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Vision

ABSA, the leader in the profession of biological safety.

Mission Statement

The American Biological Safety Association is dedicated to expanding biological safety awareness to prevent adverse occupational and environmental impact from biohazards.

Goals

- Expand professional and public awareness of biological safety through effective communication.
- Participate in the development of biological safety standards, guidelines, and regulations.
- Develop ABSA as the recognized resource for profession and scientific expertise in biological safety.
- Advance biological safety as a scientific discipline through education, research, and professional development.
- Develop and maintain standards for biological safety professionals.

About the Cover

The cover illustration is a computer-generated graphical representation of the crystalline structure of the Foot-and-Mouth Disease Virus (FMDV), generously provided by Richard Meyer and Fred Brown of the Plum Island Animal Disease Center. Richard Meyer is currently at the Centers for Disease Control and Prevention. Information on FMDV may be found in a brief review of this topic in the Special Features section of this issue.
I attended my first biological safety conference in 1981 in Athens, Georgia. As a graduate student in Dr. Jerry Tulis' Biohazard Science Program at UNC-CH, I was in awe of the experts I was able to meet at that meeting. Only a few years after the original NIH recombinant DNA Guidelines were developed, and before the first draft of the "BMBL," I was introduced to the experts—Dr. Emmett Barkley, Dr. John Richardson, Dr. Everett Hanel, Manny Barbeito, and others who were willing to take some novice students under their wings. I learned that being a biosafety professional meant being highly motivated and unselfish, willing to take time to encourage and teach students and others new to the biosafety field. I watched the sharing of experiences with other well-seasoned colleagues at the annual conferences. I learned that if you wanted to know something, you picked up the phone and called, and someone would help you find the answer.

In fact, phone calls and the annual conference were the primary means of biosafety communication. In 1984, biosafety professionals came together formally with the birth of the American Biological Safety Association (ABSA). In the mid-80s, the first ABSA newsletter was published with Dr. Jerry Tulis as the editor, and it became the first attempt at formal, routine communications among members. One of the greatest accomplishments of ABSA was the publication of the Journal of the American Biological Safety Association (JABSA) in 1996, with Dr. Mel First as the first editor. The Journal was born out of the goals of ABSA to provide effective communication among ABSA members, expand professional awareness of biological safety, and advance the profession as a scientific discipline.

We've watched ABSA grow over the past 17 years, along with the scope of the field of biosafety. No longer does our field consist solely of laboratory safety specialists. Now we see our influence in the pharmaceutical industry, frontline healthcare, shipping and transport, international issues, and safety product and device industries. The widespread use of the worldwide Web has assisted us in many ways with instant information, but we find we need direction and guidance to distinguish between irrational perceptions and discerning risk analysis.

We are learning to adapt to our new growth and needs. Based on input from ABSA members, our Publications Committee, under the leadership of Dr. Joe Van Houten, reviewed the impact and use of the Journal with the intent of building on the foundation of a scientific document for biosafety professionals. A new journal name, a new look, and a new format are the results of several years of discussions. Applied Biosafety now includes not only full manuscripts and chapters, but updates on new guidelines and regulations, published responses from ABSA to revised or proposed guidelines (thanks to Bill Homovec and the Technical Review Committee), helpful hints for using the Web or for developing training programs, and a broad range of topics from environmental microbiology to bloodborne pathogens. We owe a debt of gratitude to Drs. Richard C. Knudsen and Ira F. Salkin (Co-Editors) and the other Journal publication staff for tackling this challenge and producing such a fine product.

Hopefully, the expanded interests and issues of the members of ABSA are reflected in this new journal format. In keeping with the honorable biosafety tradition of sharing our experiences and teaching others, let's remember to contribute to our Journal. The Publications Committee has provided us with ample opportunity to do so.
Richard C. Knudsen  
Centers for Disease Control and Prevention, Atlanta, Georgia

The objective of a biosafety program is to protect personnel and the environment from exposure to an infectious agent. It is not often that we have a concrete example of “protecting the environment” so aptly presented to us by the multimedia press. If you watch TV, read a daily newspaper or weekly news magazine, you should be well aware that Foot-and-Mouth Disease (FMD) is wreaking havoc in Great Britain and Western Europe. FMD is a disease of cloven-footed animals, which includes livestock such as cattle, swine, sheep, and goats. Livestock and their fields, pastures, feedlots, barns, farms etc., as well as the surrounding air, constitute the “environment.” FMD is caused by a tiny virus, Foot and Mouth Disease Virus (FMDV; see cover illustration). FMDV can survive in the environment for days or weeks where it can continue to serve as a source of infection. Since FMDV does not infect humans and most adult animals usually recover, what’s the big deal with this virus?

Cattle, swine, sheep, and other livestock animals are economic powerhouses for the domestic economy and international markets in many nations in the world. There is a huge international business in exporting/importing meat, milk, and cheese products, animal hides, and many other animal products throughout the world. It has been estimated that the annual export market for animal products for the U.S. is $60 billion. If one animal on a single farm on the U.S. mainland is diagnosed with FMDV, the country’s exports of animal products could be shut down for 6 months or more. Add on the many costs of control and eradication of the disease, compensation costs for farmers etc. and we can see that the disease can have a tremendous domestic and international economic impact. For example, the 1997 outbreak in Taiwan may have cost as much as $5 billion.

The United States has not had an outbreak since 1929, but in the last 12 months outbreaks have occurred in at least 23 nations in the world, not including those in Western Europe. These nations include Brazil, Colombia, Japan, and Russia. The United States could be next on the list.

A worst case scenario would be an FMD outbreak in the U.S. traced to the virus escaping from a U.S. laboratory. To minimize this possibility laboratory work with FMDV is confined to the United States Department of Agriculture’s Plum Island Animal Disease Center (PIADC), located off the eastern tip of Long Island, New York. The isolated island location, enhanced BSL-3 facilities, and tight security restrictions on personnel minimizes any possibility of aerosol or other transmission to mainland animals. PIADC is an ideal example of a laboratory designed and operated for protecting the environment against the escape of an infectious disease.

To learn more about this economically devastating disease read the article “Foot-and-Mouth Disease: A Brief Review of the Etiologic Agent and the Disease Which It Causes” in this issue’s Special Features section.
Comparative Analysis of the Methods for Determining the Efficiency of Air-Purification Filters Using Dioctyl Phthalate and Turbine Oil Aerosols


State Research Center of Virology and Biotechnology Vector, Kotlovso, Novosibirsk Region, 630559, Russian Federation

Abstract

The methods for determining the efficiency of domestic fine air-purification filters using dioctyl phthalate and turbine oil test aerosols were compared under actual working conditions. The filters used were of different sizes and employed different filter materials. Such filters are used in the State Research Center of Virology and Biotechnology Vector and other similar institutions of Russia for facility air purification and respiratory protective equipment for researchers and technicians involved in manufacturing diagnostic, medicinal, and prophylactic preparations and performing research of group I-IV human-pathogenic viruses. No significant differences between the permeability coefficients of these filters tested by dioctyl phthalate and turbine oil aerosols were recorded. The data demonstrate that both dioctyl phthalate and turbine oil aerosols are equally appropriate for testing air-purification filter efficiency.

Introduction

Different types of fine filters are presently used for efficient air purification in ventilation and engineering systems at medical and microbiological production enterprises and research institutions involved in studying pathogenic microorganisms. Different methods and test aerosols are used for monitoring the efficiency of these filters (Drozdov et al., 1987; White & Smith, 1967), different countries preferring different methods. In the United Kingdom, the standard method for filter testing requires methylene blue aerosol (Boyne, Dymant, & Thomason, 1971); in the USA, dioctyl phthalate (DOP) (Dorman, 1967); and in Germany, turbine oil aerosol (Dorman, 1968). As for Russia, the method for gas mask testing based on turbine oil mist is one of standard methods (Russian State Standard GOST).

The retentive efficiency of Russian filters used in ventilation systems, containment areas, and personal protective equipment (PPE) in the State Research Center of Virology and Biotechnology Vector (SRC VB Vector) while developing and manufacturing diagnostic, medicinal, and prophylactic preparations and performing research on group I-IV human-pathogenic viruses, including special pathogens (smallpox virus, Ebola, Marburg, etc.), is tested using oil mist. The efficiency of fine HEPA (high efficiency particulate air) filters, used in the United States in similar institutions for analogous purposes, is tested using DOP aerosol (Standard 49, NSF International; Standard IES-PRCC-001-83).

The object of this study was to compare the methods for determining the efficiency of domestic air-
purification filters of different types under actual working conditions at the SRC VB Vector using DOP and turbine oil aerosols.

**Experimental Conditions**

The turbine oil grade Т₂₂ or Т₃₀—a liquid mixture of hydrocarbons, mainly, alkynaphthenes and alkylaromatics, with a high boiling point (Т₅ = 300° - 600° C)—is used in Russia as a mist-forming substance. The turbine oil is produced during oil refining and contains antioxidants, anticorrosives, antifoam additives, and demulsifiers. For comparison, DOP produced by Sigma-Aldrich (USA) was used. An oil mist consisting of a fine particulate aerosol of these substances was produced using a small-scale unified condensation aerosol generator GAK-UM (Russia). Concentrations of the aerosols produced were determined in a standard photometer FAN-A UkhL-4, 2 (Russia) with a measurement range 10⁰ - 10⁷ particles/m³.

The efficiencies of individual filters and ventilation chambers housing banks of filters were evaluated according the protocol below. A schematic representation is provided in Figure 1.

**Figure 1**

Scheme of the unit for testing filters and ventilation chambers using turbine oil and DOP mists:
(1) airtight valves; (2) generator GAK-UM; (3) supply-pipe for delivering aerosols; (4) ventilation chamber (filter); (5) tank; (6) peristaltic pump; (7, 8) sampling exhaust-pipes; (9) photometer; (10) vacuum pump; (11) rotameters; (12) couplings; and (13) ventilator.

**Testing Technique**

Prior to testing, airtight valves I of the air duct were closed. The agents tested (turbine oil and DOP mists) were generated for 2 - 5 min from generator 2 into the air duct through supply-pipe 3 until the initial concentration prior to the filter 4 reached 10⁶ - 10⁷ particles/m³. Particle concentration was measured using photometer. To produce the mist, oil or DOP was supplied to the generator GAK-UM from tank 5 using peristaltic pump 6 (Gilson, France), with a capacity of 5 - 8 ml/min, simultaneously with compressed air under a pressure of 3 atm (the compressed air is required for both production of the aerosol and its delivery to the air duct). When the required initial concentration prior to the filter was reached, the airtight valves were
Comparison of Filter Testing Methods

opened, and the agents tested passed through the filter. The air samples collected before (exhaust pipe 7) and after the filter (exhaust-pipe 8) were transported to photometer 9 to determine the mist concentrations. Pump 10 (Sartorius, Germany) facilitated the transfer of the air samples through the test system.

Results

Filter permeability coefficient ($K_p$) was calculated according to the following equation:

$$K_p = \frac{I_2}{I_1} \times 100\%,$$

(1)

where $I_1$ is the light scattering corresponding to the aerosol concentration prior to the filter, $\mu A$, and $I_2$, after the filter, $\mu A$.

The value of light scattering is proportional to mist concentration; therefore, we omitted the conversion to concentration value. Thus,

$$K_p = \frac{I_2}{I_1} \times 100\% = \frac{C_2}{C_1} \times 100\%,$$

(2)

where $C_1$ is the mist concentration prior to the filter, particles/m$^3$, and $C_2$, particles/m$^3$, after the filter.

Each individual filter or cascade of ventilation chamber is considered serviceable if its $K_p$ does not exceed $1.0 \times 10^{-3}\%$.

To further validate the comparison of filter retention when challenged with turbine oil and DOP, the particle size composition of these aerosols, produced under identical conditions in the generator GAK-UM, was studied and compared during the initial stages of the research project. A four-stage Andersen cascade impactor BP-35/25-4 (Russia) was used in this part of the study. To exclude the loss of the finest particles, an AFA-BA filter was used as an additional fifth stage. At an airflow volume of 25 l/min through the impactor, the four stages of the impactor retained 50% of the particles, with mass median aerodynamic diameters (MMAD) of 12, 6, 2.1, and 0.8 $\mu m$, respectively. All impactors were certified and calibrated using a monodisperse aerosol generator with vibrating orifice Berglung-LIU (TSI, USA) prior to conducting tests with turbine oil or DOP. Testing in a ROYCO (TSI, USA) multichannel photoelectric particle counter demonstrated that the aerosol produced consisted of fine particulate aerosol.

The data demonstrate that MMAD$_{50}$ for the DOP aerosol particles ranged between 0.19 - 0.36 $\mu m$; for turbine oil particles, 0.17 - 0.34 $\mu m$; $\mu p_{50} = 1.5 - 2.0$ (geometric standard deviation, characterizing the range of particle sizes in aerosol). In both DOP and turbine oil aerosols, 97.7 $\pm$ 2.3% and 98.6 $\pm$ 2.3% of the particles, correspondingly, fell into this size range.

Thus, the experimental data obtained have demonstrated that the DOP and turbine oil aerosols produced through nebulizing in the generator GAK-UM display essentially the same particle size composition ($P<0.05$). We proceeded with the second stage of the work.

Discussion

Standard, domestically produced, highly efficient filters of different types (Table 1) (Gaponov, 1981) were selected for comparative testing. Filters FETO-750, FTO-1000, FTO-500, and FTO-60 are routinely installed in microbiological laboratories and production facilities in the systems for ventilation and air purification. Filters of another type, FTO-S-500K, are used in the systems supplying compressed air and autoclave vacuum of the entrance through autoclaves. These filters are capable of filtering moisture air and retain their filtration capacity after steam sterilization. Gas mask filters EO-15 and filters V-0.4 are designed for use in PPE, such as individual protection suits (suits "L-1," "Korund," and pneumatic suits). Note also that the EO-16 filter contains another filtering material—activated charcoal—and, therefore, this was another reason to include these filters into our study.

Our main attention was focused on testing the filters installed with the systems purifying the facility air that was exhausted from both level II (BSL-3) rooms (Drоздов et al., 1987) within single cascade ventilation chambers and level III (BSL-4) within dual in-line filter ventilation chambers. The efficiency of each single cascade was tested individually; for dual in-line cascade chambers, the data were pooled. The airflow capacity for each individual ventilation chamber or filter was determined under actual working conditions within the corresponding engineering systems installed in different buildings of the State Research Center of
## Table 1
Types and Main Characteristics of the Filters for High Efficient Air Purification

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<tr>
<th>Type of filter or filtration unit</th>
<th>Material</th>
<th>Characteristics</th>
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<tr>
<td>FTO-750 (filtration unit for fine air purification with a capacity of 750 m³/h), V-0.4</td>
<td>FPP-15-1.5; FPP-15-4.5 (Petryanov’s polyvinyl chloride filter with a fiber diameter of 1.5 and 4.5 μm, respectively)</td>
<td>Polyvinyl chloride fibers on a gauze base; thermostable at 60-70°C, hydrophobic</td>
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<tr>
<td>FTO-60, FTO-500, and FTO-1000 (fine filters with a capacity of 60, 500, and 1000 m³/h, respectively)</td>
<td>FPAN-10-3.0 (Petryanov’s acryl nitrile filter with a fiber diameter of 3.0 μm)</td>
<td>Polyacryl nitrile fibers on a gauze base; thermostable at 180°C</td>
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<tr>
<td>FTO-S-500 (sterilizable fine filter)</td>
<td>Basalt paper and board</td>
<td>Superthin basalt fiber with addition of cellulose</td>
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<tr>
<td>EO-16 (gas mask filter)</td>
<td>Activated charcoal</td>
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Virology and Biotechnology Vector. The results of the testing are shown in Table 2 (single cascade ventilation devices and individual filters) and Table 3 (dual in-line cascade ventilation chambers).

The $K_p$ values of domestic filters, installed in various engineering systems, were virtually equal when results were compared following challenge with DOP and turbine oil (Tables 2 and 3). Analysis of the data obtained has demonstrated the correlation between the permeability coefficients of the test aerosols used (Batova & Motina, 1977; Lakin, 1980). The correlation coefficients calculated demonstrate a strong and reliable correlation between the indices compared.

We have demonstrated that both DOP and turbine oil have virtually equal particle size composition and are equally suitable for producing test aerosols for determining the efficiency of various domestic filters used for air purification.

### References


## Table 2
Efficiency of Single Cascade Filtration Devices Tested with Turbine Oil and DOP Aerosols

<table>
<thead>
<tr>
<th>System and type of installed filter</th>
<th>Number of filters in the system unit under testing</th>
<th>Capacity of system, m³/h</th>
<th>Permeability coefficient with respect to turbine oil mist, (X±J₉₅)×10⁻³, %</th>
<th>Permeability coefficient with respect to DOP mist, (X±J₉₅)×10⁻³, %</th>
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</tr>
<tr>
<td>----------------------------------------------------------------------------</td>
<td>---------</td>
<td>---------</td>
<td>---------</td>
<td>---------</td>
<td>---------</td>
</tr>
<tr>
<td>Exhaust ventilation of III class virological cabinets, FTO-60</td>
<td>0.023±0.005</td>
<td>0.022±0.005</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exhaust ventilation of II class virological-biochemical cabinets, FTO-1000</td>
<td>0.110±0.002</td>
<td>0.012±0.002</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Autoclave vacuum, FTO-500, FTO-S-500K</td>
<td>0.002±0.001</td>
<td>0.002±0.001</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exhaust air filtration of sewage-collecting collecting tanks, FTO-60</td>
<td>0.037±0.021</td>
<td>0.050±0.026</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exhaust filtration of specialized plumbing (internal sewage system), FTO-60</td>
<td>0.230±0.084</td>
<td>0.163±0.023</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Individual PPE filtration systems in protection suit, V-0.4</td>
<td>0.033±0.024</td>
<td>0.030±0.015</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Individual PPE filtration system in gas mask, EO-16</td>
<td>0.099±0.049</td>
<td>0.109±0.086</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: Five measurements were made for each filter or ventilation chamber in lines 1-7; six, in lines 8-9.
* II zone according to the Russian classification corresponds to BSL-3.
Comparison of Filter Testing Methods


Russian State Standard GOST 32-74.

Russian State Standard GOST 10189-62.


Standard IES-PR-CC-01-83, USA.


Table 3
Efficiency of Dual In-line Cascade Ventilation Chambers of Exhaustive Ventilation Tested with Turbine Oil and DOP

<table>
<thead>
<tr>
<th>Number of filters in dual in-line cascade ventilation chamber</th>
<th>Capacity of system, m³/h</th>
<th>Permeability coefficient with respect to turbine oil mist, ((X\pm J_{95})\times10^{-3}, %)</th>
<th>Permeability coefficient with respect to DOP mist, ((X\pm J_{95})\times10^{-3}, %)</th>
<th>Correlation coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>8 (2 cascades with 4 filters in each)</td>
<td>3000</td>
<td>0.212±0.021</td>
<td>0.205±0.021</td>
<td>1.0</td>
</tr>
<tr>
<td>24 (2 cascades with 12 filters in each)</td>
<td>8300</td>
<td>0.120±0.011</td>
<td>0.125±0.031</td>
<td></td>
</tr>
<tr>
<td>16 (2 cascades with 8 filters in each)</td>
<td>3000</td>
<td>0.130±0.021</td>
<td>0.133±0.021</td>
<td></td>
</tr>
<tr>
<td>16 (2 cascades with 8 filters in each)</td>
<td>5000</td>
<td>0.573±0.110</td>
<td>0.538±0.113</td>
<td></td>
</tr>
</tbody>
</table>

Note: Five measurements were made for each ventilation chamber.
Introduction

The last case of smallpox occurred in 1978, not in Africa, but in Birmingham, England, transmitted by aerosol from a smallpox laboratory to a person working in a nonlaboratory area of the building (World Health Assembly, 1980). Two persons died: the index smallpox case and the director of the laboratory, who took his own life.

The eradication of polio is now within sight. As with the smallpox virus, the last remaining posterradication reservoirs of wild polioviruses will be in the laboratories of the world. In May 1999, the World Health Assembly (WHA) recognized the consequences of accidental transmission of wild poliovirus from the laboratory to the community and resolved to link Regional certification of polio eradication to progress in laboratory containment (World Health Assembly, 1999).

The first steps toward poliovirus laboratory containment are already underway in the WHO Western Pacific (WPR) and the European (EUR) Regions. The WPR anticipated being certified as polio-free in the year 2000 and the EUR in 2001. Both Regions have begun the process of surveying all laboratories that might possess poliovirus infectious and/or potentially infectious materials and creating agency/institutional, national, and Regional inventories of laboratories that retain such materials.

The American Region (AMR) was the first Region to be certified as polio-free in 1994, before the WHA containment resolution. The AMR now faces the challenge of preparing for high containment by completing the national laboratory surveys and inventories over the next few years, in advance of global certification. The Global Commission for Certification of the Eradication of Poliomyelitis has advised that destruction or transfer of all wild poliovirus infectious materials to high level containment facilities must be implemented worldwide before global certification of eradication can be achieved. Finding laboratories that may possess wild poliovirus in the developing countries of the Region will be relatively straightforward. Their numbers are few and locations well known. Finding such laboratories in the more developed countries will be more complicated. A large number and wide variety of biomedical control, diagnostic, production, research, and teaching laboratories have worked with known and unknown wild poliovirus infectious materials over the past 60 years. These laboratories may be located in public health, environmental control, and defense agencies; hospitals; universities; and research institutions. Meeting the enormous and complex challenge of wild poliovirus containment requires the full support of nations at all levels of government.

Risk of Wild Poliovirus Escaping from the Laboratory

"Escape from the laboratory" is an unfortunate term, widely used in the media, which conveys the image of a malevolent microorganism flying or crawling from its prison laboratory freezer, intent on wreaking havoc on mankind. This popular, sensationalized image is mentally difficult to overcome. Reality is more mundane. Transmission of wild poliovirus from the laboratory to the community will occur only through human frailty, that is, by someone deliberately or accidentally working with infectious or potentially infectious materials under inappropriate or unsafe conditions.

The World Health Organization (WHO) defines
infectious materials as wild poliovirus isolates, reference strains, research derivatives with wild virus capsid sequences, clinical specimens from confirmed or suspected cases, infected experimental animals, and environmental sewage or water samples known or suspected to be contaminated (World Health Organization, 2000). Potentially infectious materials are defined as throat swabs, feces, and environmental samples collected for any purpose at a time and in a geographical area where polio was known or suspected to be present and maintained under conditions known to preserve the virus.

Poliovirus infections may be acquired through breathing contaminated aerosols or droplets, ingesting contaminated food or water, or placing contaminated objects in the mouth (Melnick, 1996). High doses of poliovirus are more likely to cause infection than low doses, particularly among persons with waning mucosal immunity. Thus, products of the poliovirus laboratory present a much greater risk than clinical materials. Poliovirus grown and manipulated in the laboratory for diagnostic or research purposes may contain 1,000 to 1,000,000 more virus particles than equal volumes of clinical materials. Working in the laboratory was recognized early in the prevaccine polio research era as presenting a much greater hazard than providing clinical care (Wenner & Paul, 1947).

Risks from potentially infectious materials collected from polio endemic regions for studies, for example, in bacteriology, parasitology, or nutrition laboratories, are likely to be very small, but not zero. The rationale for including potentially infectious materials on the list for containment stems from the high rate of subclinical to clinical (100 - 1,000 to 1) poliovirus infections (Melnick, 1996). During the polio high season in endemic countries, many children will be infected but not ill. Thus, some of the throat or stool specimens collected for other purposes may unknowingly contain wild poliovirus. Contaminated specimens in most collections will be random, and poliovirus content low. Risks further decrease if procedures in such laboratories involve heating or chemical treatment that may inactivate the virus. Risks increase when contaminated specimens are inoculated into cells or experimental animals in which unsuspected wild polioviruses may also replicate.

Transmission of poliovirus from the laboratory to persons outside the laboratory through contaminated sewage effluents, solid wastes, or spent unfiltered air is theoretically possible, but difficult to document against a background of high level immunity in the population. Also, there is no direct evidence of the infection of others through contaminated skin or the clothing of laboratory workers. More readily documented has been disease among laboratory workers.

Twelve laboratory-acquired cases of poliomyelitis were reported from 1941 through 1976, all with potential for virus transmission to the community (World Health Organization, 2000). That no cases of polio among laboratory workers have been reported since 1976 testifies to the effectiveness of attenuated oral polio vaccine (OPV) and inactivated polio vaccine (IPV) and major improvements in laboratory techniques, equipment, and facilities. For many years, working with wild poliovirus has raised little concern about laboratory safety because of the strong protection against the disease provided by near universal immunization of laboratory workers and the population at large.

Unknown, however, is the occurrence of poliovirus infections among laboratory workers in the absence of disease. The effectiveness of polio vaccines in preventing laboratory-associated poliomyelitis does not necessarily extend to prevention of subclinical infections (Sutter, Cochi, & Melnick, 1999). Virus shedding in saliva and stools from unrecognized subclinical infections represents a serious potential for polio transmission to the community.

Silent transmission from the laboratory to the community can occur. Van Loon and coworkers reported the recovery of a wild poliovirus from an 18-month-old son of a worker in an IPV production facility (Mulders et al., 1997). The father had been exposed to an accidental spill of preinactivated virus a few weeks before the virus was recovered from the child. The mechanism of virus transmission from the father to the child was undetermined. The authors also describe a separate incident of the isolation of a common laboratory reference strain of unknown origin from a 3-year-old child.
Consequences of Transmitting Wild Polioviruses from the Laboratory to the Community

The purpose of wild poliovirus containment is to protect the community. The immunized laboratory worker is not at risk of disease. Neither is the community at significant risk of transmission as long as high levels of polio immunization are maintained worldwide (preeradication). After virus eradication (posteradication phase), the potential for erosion of immunization levels increases with time. Inadvertent transmission and spread of the virus during this phase is likely to be interrupted, but at considerable financial and programmatic costs. Once OPV immunization stops (postimmunization phase), the public health consequences of virus transmission from the laboratory to the community assumes greater proportions with each new unimmunized annual birth cohort. Eventually a susceptible population will emerge which includes adolescents and adults who are at highest risk for the most severe consequences of infection, paralysis, and death. The potential for such an unprecedented pandemic dictates the need for increasingly stringent attention to containment in the years following cessation of immunization.

Stopping OPV Immunization

If the consequences of transmission are so great, why stop OPV immunization? For several reasons: First, continuing immunization in the absence of disease is difficult to justify and even more difficult to maintain. Second, nearly all vaccine or drug interventions carry some risks. The current Sabin OPV is associated with a risk of about one case of vaccine associated paralytic poliomyelitis (VAPP) per 2.4 million first doses of vac-

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**Figure 1**
Requirements for Laboratories Having or Working with Polioviruses

<table>
<thead>
<tr>
<th>Eradication phase</th>
<th>Pre-eradication</th>
<th>Post-global eradication</th>
<th>Post-OPV immunization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wild virus circulating</td>
<td>OPV vaccine/vaccine-derived virus</td>
<td>BSL*-2/polio</td>
<td>BSL-2/polio</td>
</tr>
<tr>
<td>BSL-2/polio</td>
<td>BSL-3/polio</td>
<td>BSL-4</td>
<td></td>
</tr>
<tr>
<td>All laboratories</td>
<td>Wild virus</td>
<td>BSL-2/polio</td>
<td>BSL-3/polio</td>
</tr>
<tr>
<td>Special circumstances</td>
<td>Public health and clinical (diagnostic tests only)</td>
<td>BSL-2/polio</td>
<td>BSL-2/polio†</td>
</tr>
<tr>
<td>BSL-2/polio</td>
<td>BSL-3/polio</td>
<td>BSL-2/polio†</td>
<td>BSL-3/polio</td>
</tr>
<tr>
<td>Vaccine production</td>
<td>OPV</td>
<td>BSL-2/polio</td>
<td>BSL-2/polio†</td>
</tr>
<tr>
<td>IPV</td>
<td>BSL-2/polio</td>
<td>BSL-3/polio</td>
<td>BSL-4†</td>
</tr>
</tbody>
</table>

* Biosafety level (see Box 9)
† No live wild virus controls used in diagnostic or reference tests.
‡ Maximum containment in vaccine production facilities will be addressed on a facility-by-facility basis.
** No live virus controls used in diagnostic tests.
Biosafety Implications of Polio Eradication

cine (Sutter, Cochi, & Melnick, 1999). VAPP was of little consequence when paralytic polio in the United States reached as much as 20,000 cases annually. But in the absence of epidemic polio for more than 20 years, the 4 to 8 VAPP cases each year became increasingly unacceptable. In the year 2000, the United States joined Canada and many Western European countries in recommending only IPV in its routine immunization schedule.

OPV continues to be essential for eradication in polio endemic countries because of its cost, ease of administration, and superior immunizing qualities. With each passing year after polio eradication, VAPP in developing countries will be more readily recognized and difficult to defend. Just as vaccine policy evolved away from OPV in the United States, the developing countries should expect no less. The appropriate strategy for stopping OPV immunization worldwide is the subject of current research. Whether stopping will be a synchronized regional or worldwide effort, with or without replacement by IPV for a limited time, is yet to be decided. The probability is high that OPV immunization will stop globally when it can be assured that wild poliovirus has been eradicated, that no OPV derived viruses are freely circulating, and wild polioviruses are contained in the laboratory (World Health Organization, 1998).

No laboratory is asked to destroy programmatically important viruses at this time, only that laboratories retaining wild poliovirus infectious and potentially infectious materials are listed on national inventories and meet the progressively stringent containment standards. Similarly, the identification of potentially infectious specimens need not culminate in the destruction of valuable research materials, but appropriate action should be initiated to complete studies on the materials, test for polioviruses, treat to inactivate polioviruses, or prepare for containment.

Action to be taken over the next few years in the Americas is a prerequisite for global certification of eradication. It includes national surveys of all biomedical laboratories, urging destruction of all unneeded wild poliovirus infectious materials, and the creation of national inventories of laboratories/agencies/institutions retaining such materials. This will be a major challenge for all nations, but particularly for those with large research institutions. Generic guidelines have been prepared by WHO to assist Regions and nations in conducting surveys and preparing inventories. The scheme is hierarchical (Figure 2). Key to its success is the full cooperation and support of national governments, agencies/institutions, and the laboratories under their jurisdiction. At each of these levels, the role of the biosafety community is crucial.

Conclusions

There are those who maintain that it will be easier to eradicate wild poliovirus in nature than in the laboratories of the world. The former can be verified. The latter cannot.

However, time is on our side. The step-wise process of national sensitization to the challenge begins now with the national survey and inventory of laboratories retaining wild poliovirus infectious and potentially infectious materials. Containment comes to the forefront again in 2 to 3 years when the wild virus in nature has been eradicated and the same laboratories are requested to implement high containment. The third opportunity to review compliance will occur in 5 to 10 years when decisions will be made on how and when to stop OPV immunization. Adequate evidence of wild polioviruses being present in a limited number of laboratories and under maximum containment will be key to that decision.

Attrition among the laboratories retaining wild polioviruses is expected with each containment phase. Moving from good laboratory practices to high containment represents a major investment in facilities, maintenance, and personnel, and an increasing national responsibility for safety. Moving from high to maximum containment represents still another major step in national investment and responsibility. At some point, nations and institutions will have to weigh the high costs of containment against the value of retaining a virus of no diagnostic or public health value.

As with smallpox, global surveillance for wild polioviruses will continue through the WHO Poliovirus Laboratory Network for many years after eradication. A polio vaccine stockpile and rapid response emergency plan will provide further insurance against the initial uncertainties of laboratory containment, bioterrorism, and reemerging virus. The polio eradication effort grew out of an unprecedented spirit of support among all na-
Figure 2
Developing the Global Inventory of Wild Poliovirus Infectious and/or Potentially Infectious Materials

WHO requests member countries to begin Nation-wide laboratory search

Countries (MOH appoint Coordination Group to oversee and monitor containment procedures

Coordinating Group works with ministries to identify agencies/institutions

National certification committee reviews plans

Agencies/institutions request laboratories to search facilities

Laboratories document the absence of such materials or list such materials

REGIONAL INVENTORY

NATIONAL CERTIFICATION COMMITTEE

NATIONAL INVENTORY

AGENCY/INSTITUTIONAL INVENTORY

LABORATORY INVENTORY
Biosafety Implications of Polio Eradication

ations, public and private organizations, and people at all levels all over the world. There is every reason to assume that this spirit of collaboration will continue and within a few years the risk of transmission of wild poliovirus from the laboratory to the community will no longer exist.

References


Risk Assessment for Working with Infectious Agents in the Biological Laboratory

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Centers for Disease Control and Prevention, Atlanta, Georgia

Abstract

Seventeen risk factors for working with infectious agents in the laboratory and animal facility environment are identified and discussed. The risk factors are useful in performing qualitative risk assessments to determine the biosafety level necessary to work safely with an infectious agent or to initiate modifications to the practices and procedures, equipment and facility requirements at each biosafety level.

Introduction

Workers in biological laboratories are potentially exposed to the risks, or hazards, of infectious agents and their toxins which can cause them serious harm or death (Collins, 1983; Sewell, 1995; Sulkin & Pike, 1949, 1951; Sullivan et al., 1978). To work with these biohazardous agents, the risk of exposure to them during the work process must be assessed. This process is called risk assessment and requires the identification of the various risk factors. Each risk factor must be evaluated and then processes and controls implemented which will minimize, to the lowest possible degree, exposure to the biological agents. This latter process is risk management. Risk assessment and risk management go hand-in-hand and may be viewed as the two sides of the same coin.

Assessing the Biosafety Levels

The risk assessment process for working with infectious agents in laboratory or animal facilities is aimed at reducing to a minimum the risk of working with these agents by placing the agent in any one of four biosafety levels (BSLs), termed BSL 1, 2, 3, and 4, as defined by the CDC/NIH guidelines Biosafety in Microbiological and Biomedical Laboratories (BMBL) (Richmond & McKinney, 1999). Each biosafety level has specific facility, equipment, and practice requirements for working with the assigned infectious agents. The risk assessment process is also used for enhancing or modifying facility, equipment, and usually the practices and procedures at each biosafety level. Some examples include the use of BSL-3 practices with BSL-2 facilities, the use of high efficiency performance (HEPA) filters on BSL-3 laboratory air exhaust systems, and the addition of waste treatment and shower out facilities to BSL-3 laboratories when working with USDA-restricted animal and poultry pathogens. A complete discussion of the four biosafety levels is found in the BMBL.

BSL-1 is appropriate for work with defined and characterized strains of microorganisms that are not known to cause disease in healthy adult humans. BSL-2 is appropriate for a broad spectrum of indigenous moderate-risk agents present in the community and associated with human disease of varying severity. BSL-3 is appropriate for work with indigenous or exotic agents with a potential for respiratory transmission, and which may cause serious and potentially lethal infection. BSL-4 is appropriate for dangerous and exotic agents which pose a high individual risk of life-threatening disease which may be transmitted by the aerosol route and for which there is no available vaccine or therapy.
Qualitative vs. Quantitative Risk Assessment

Risk assessments can be either quantitative or qualitative. The most effective risk assessments are quantitative, or measurable, and are often used for those chemical hazards or radiological hazards which can be readily measured. However, biological agents are not uniform chemical moieties for which well developed and relatively easy-to-perform assays are available. They are a complex of thousands of interreactive biochemical macro and micro molecules such as proteins, lipids, carbohydrates, nucleic acids and their building blocks united into discrete units which have the capacity to reproduce themselves in the host's cells, tissues, and body fluids. There is also an incredible variety of infectious agents, ranging from bacteria, rickettsia, viruses, yeasts, molds, uni- and multicellular parasites, and prions. Each species of agent may have subtypes, strains, and variants that differ from the parent in virulence, host range, transmission, sensitivity to antimicrobial agents, etc. Because of their chemical complexity and biological diversity, no single chemical test can be used to identify a particular species of microorganism much less its related variants and subtypes.

The most defining characteristic of an infectious agent is its ability to replicate in the host (Knudsen, 1999). Viruses and rickettsia can only replicate in living cells. Bacteria, yeasts, and molds can replicate in extracellular spaces and body fluids. Damage to the host is not caused by the initial invading microbes but by their descendants, replicated many thousands or millions of times over in the host and oftentimes spreading to other organs and tissues for further replication. Thus, the most quantitative measure of an infectious agent is its ability to replicate. However, assays of replicability are difficult to perform, time-consuming, costly, and can be used only for a limited number of agents. Because such assays are usually done in vitro or in surrogate cells or animal hosts, they are also subject to considerable interpretation when trying to extrapolate these results to the human host.

It is the biological diversity of microorganisms, their complex chemical structure, their multiple methods of transmission, their complex interactions with the host, and their unique requirement to replicate within the host that make it difficult to define meaningful assays that might be used to identify them in quantitative assays. Because quantitative risk assessments cannot usually be adequately performed, it is necessary to rely on qualitative risk assessments.

Qualitative Risk Assessment: Risk Factors

The following paragraphs discuss the major risk factors that are normally encountered in working with infectious agents in the laboratory environment. Some of these risk factors, such as disease severity, transmission mode, and availability of prophylactic measures, are critically important in determining the biosafety level. Other risk factors are important for suggesting areas where additional protective measures are needed within the biosafety level.

Agent Identity and Characterization

The identity of an agent is the key to the information-gathering process. If the identity of the agent is known or strongly suspected, it can be determined if it is a well characterized or a poorly characterized agent. If the agent is well characterized published disease information (Benenson, 1995), agent summary statements, and recommended biosafety levels (or risk groups) will be available (Kennedy, 1996; Richmond & McKinney, 1999; USDHHS, 1994). The history of laboratory-acquired infection with the agent may be well documented in the literature and review articles (Collins, 1983; Sewell, 1995; Sulkin & Pike, 1949, 1951; Sullivan et al., 1978). If the agent is suspected, such as Mycobacterium tuberculosis in a sputum specimen from a suspected TB patient, we should treat the specimen as if it did contain TB. Caution should always be exercised when working in the laboratory with known and well characterized agents that might have originated from epidemics, or that might be resistant to antimicrobial agents.

If the agent is known, but it is poorly characterized, the risk assessment process will be more difficult because of the lack of published information. Examples of such agents may be found in a 1997 review of infectious diseases by Mahy (1997) who listed 42 new viruses and
four new rickettsia discovered since 1988. Because the agent is known, information on related microbial family members and other published disease observations may be available. The clinical signs and symptoms of disease and inferences on transmission characteristics by medical practitioners may also have to be relied on.

The most difficult assessment occurs when the agent is unknown because there is little or no information available. Initial outbreaks of hantavirus infection (CDC, 1994) with pulmonary syndrome, and Hendra and Nipah viruses (CDC, 1999) are examples where the infecting agent was initially unknown and uncharacterized. Under these circumstances information from field outbreaks, and servicing medical practitioners, might be the only available information. Because so little is known about the transmissibility of these unknown agents naturally and in the laboratory, the risk to the laboratory worker is higher.

Pathogenicity

Pathogenicity is the ability of an agent to cause disease and varies with the subtype, strain, or antimicrobial resistance of the infectious agent. For example, there are pathogenic and nonpathogenic strains of Ebola virus, Escherichia coli, and Bacillus anthracis (anthrax). Ebola Zaire is highly pathogenic for humans whereas Ebola Reston does not appear to cause disease in humans although it does in primates. Escherichia coli is a normal member of our intestinal flora; however, E. coli strain 0157H7 is a deadly pathogen. The difference between pathogenic and nonpathogenic strains of anthrax is dependent on the presence of a plasmid in virulent strains. Many agents, such as Clostridium botulinum, depend on the secretion of toxins for their pathogenicity.

Virulence

Virulence is the degree of pathogenicity. Virulence depends on the infectivity of the agent and the severity of disease (which will be discussed in a following paragraph). Some disease isolates may require a lower infectious dose (discussed in a following paragraph) and will be more transmissible, more invasive, and more severe than other isolates. Neisseria meningitidis is endemic in our population, but epidemics occur and isolates from these epidemics might be more transmissible or more invasive than endemic strains. Endemic and epidemic strains of influenza would be another example. Virulence can also vary with the route of infection. When inhaled, anthrax spores can cause a fatal pneumonia, but if introduced into the skin the spores will cause a cutaneous lesion. Unless the virulence of the isolate or strain is known with certainty, it is best to assume that the strain is pathogenic and virulent.

Infectious Dose

It would be ideal to have accurate data on the infectious dose for every route of infection for every human pathogen. Unfortunately, infectious dose data for human pathogens, obtained from studies on human volunteers, are rare. Infectious dose data for human pathogens obtained from studies on experimental animals may or may not have close relevance to humans. Generally, those agents with the lowest infectious dose, such as Q fever with an infectious dose of 10 for humans by the aerosol route, Venezuelan equine encephalitis with an infectious dose of 1 for humans by the subcutaneous route, or measles with an infectious dose of 0.2 for humans by intranasal spray (Collins, 1983), are the greatest risks for laboratory transmission. Dilute samples of infectious agent with low infectious dose (e.g., 1-10 microorganisms) can be more hazardous than concentrated samples with a high infectious dose (e.g., 1,000-5,000 microorganisms). Agents with low infectious doses, therefore, pose a higher risk of transmission. When this information is available, it may be very valuable in the risk assessment process.

Severity of Disease

The more severe the infectious disease the higher the risk for the laboratory worker and usually the higher the biological safety level for working with the agent. Staphylococcus aureus, which can normally be found on human skin, can also cause a wide variety of diseases in humans which are generally moderate in nature and can usually be treated with antibiotics, is classified as a BSL-2 agent. Although anthrax can cause a severe to lethal disease in humans and can be transmitted by the aerosol route, it is classified as a BSL-2 agent when working with clinical specimens and
as a BSL-3 agent when working with the purified agent because of its susceptibility to antibiotics. Ebola virus, which may also be transmitted by the aerosol route in the laboratory, can cause lethal disease (up to 90% mortality) for which there is no known effective treatment and is classified as a BSL-4 agent. On the other hand, strict bloodborne pathogens which can also be lethal, such as HIV and HBV, are classified as BSL-2 agents because of their lack of transmissibility by the aerosol route.

**Regulatory Requirements**

Regulatory requirements for working with infectious agents in the laboratory (as opposed to transportation) are based on the institutional, geographical, and host origins of the agent. If the agent or the material that contains it originates in a foreign country and it is a human pathogen, it will require an import permit from the CDC (USDHHS, 1985; Richmond & McKinney, 1999). If the agent is a livestock or poultry pathogen, it will require a permit from USDA/APHIS (USDA, 1999) to import it and any materials that might contain it and to transfer it domestically. The domestic transfer of a number of human agents and toxins, termed select agents, requires that transferring facilities be registered with the CDC and, when transferred, CDC must be notified (USDHHS, 1994). The regulatory requirements usually specify biosafety levels for working with the agents and may specify specific handling, transfer, and disposal requirements. The Occupational Safety and Health Administration has also specified practices and procedures for working with bloodborne pathogens in the laboratory (USDOL, 1991).

**Host Range**

Each infectious agent has a unique host range which may vary from a single host to a wide variety of human, animal, and insect hosts. The only known reservoir for *Neisseria meningitidis*, for example, is humans. On the other hand, Venezuelan equine encephalitis (VEE) virus is pathogenic for humans, horses, and laboratory animals and is borne by several different mosquito vectors. A wide host range may necessitate additional prevention measures. Because of its wide species range, laboratories and particularly animal facilities containing VEE-infected animals must have a strict mosquito control program in effect. Furthermore, because VEE is a pathogen for horses it is a "restricted animal pathogen" and requires a USDA/APHIS permit to import it or transfer it domestically.

**The Laboratory Sample**

The previous paragraphs have discussed the characteristics of the agent. However, the laboratory worker encounters the agent in the laboratory in the form of a sample or a series of samples used in purifying, concentrating, and identifying the agent. The sample may be a clinical specimen composed of body fluids such as serum, blood, urine, and tissues, or liquid or agar cultures of a bacteria, or viral cell cultures. As the laboratory worker works with the sample, the nature, concentration, and volume of the sample may change. For example, a clinical specimen is inoculated into broth cultures and then streaked on agar plates. Purified colonies are scraped off the plates, concentrated in a centrifuge, resuspended in buffer, and then pipetted into microculture plates.

As the sample proceeds through the work process, the degree of risk to the worker changes as the nature of the sample changes. Clinical samples of blood, serum, or tissue are likely to contain lower concentrations of an infectious agent and consequently have a lowered risk of transmission. Purified, concentrated cultures of bacteria or viruses in liquid solutions pose the highest transmission risk of all because if dropped, pipetted, vortexed, or spilled the liquid material would generate splashes, splatters, micro droplets, and aerosol particles loaded with infectious particles. In general, the higher the concentration of the agent in the sample, the larger the volume of the sample; and the easier it is to aerosolize the sample, the higher the risk for the worker. The BMBL uses this concept to recommend work with clinical specimens of a number of agents such as *Neisseria meningitidis* to be performed at BSL-2, whereas work with concentrated agent preparations is recommended for BSL-3.
**Laboratory Animals**

The risks associated with laboratory animals are in proportion to the degree to which the infected animal can transmit the agent by bite or scratch, urine, feces, or by contaminated bedding or water. For example, working with experimentally infected rodent species not known to excrete the causative agent of hantavirus with pulmonary syndrome (HPS) provides a lower risk for the worker and can be performed at Animal Biosafety Level-2 (ABSL-2). On the other hand, aerosols from contaminated bedding from experimentally infected deer mice of the genera *Peromyscus maniculatus*, which are the natural hosts of HPS, should be considered a much higher risk and work should be conducted at ABSL-4 (CDC, 1994).

**Insect Vectors**

Insects provide a different kind of risk. Care must be taken to protect experimentally infected animals in animal facilities from biting insects that can transmit the disease to humans or other animals. For example, can transmit *Yersinia pestis*, the causative agent of plague, from rats to humans. Mosquitoes can transmit many arboviruses from infected animals to humans. When working with insect-borne diseases in experimental animals, the animal facility must have a vigorously enforced insect control program.

Experimentally infected insects, such as malaria-infected mosquitoes, when worked with in laboratories or insectories, can escape, and bite the handler or other workers. This work requires special containment processes, such as netting, insect traps, and special practices and procedures, such as anesthetizing and counting the mosquitoes, to reduce the risk of being bitten. At least two cases of malaria transmitted from mosquitoes to humans in research insect containment facilities have been reported to the author.

**Transmission Potential of Laboratory Activity**

Can the agent be transmitted from the laboratory sample to the worker by aerosol, ingestion, mucocutaneous exposure, or parenteral inoculation? Aerosols are considered the most hazardous mode for infectious agents because of the large number of personnel that can be infected by this route, and because most laboratory-acquired infections are known or suspected to have been caused by aerosols. Most laboratory activities, such as pipetting liquid material, shaking or vortexing containers, grinding tissues in blenders, using improper centrifuge procedures, streaking agar plates and breaking of any culture containers, have the potential for generating aerosols (Collins, 1983). Any agent that can cause upper respiratory disease, such as *Mycobacterium tuberculosis* and influenza, is a likely candidate for aerosol transmission. *Shigella dysenteriae* is transmitted in nature by ingestion of contaminated food or water and ingestion would also be the major hazard of this agent in the laboratory. On the other hand, diseases such as VEE or Rift Valley Fever that are transmitted in nature by insects are highly transmissible to man by the aerosol route when working with viral samples in the laboratory. Other agents such as human immunodeficiency virus (HIV) or hepatitis B virus (HBV) are poorly transmitted or not transmitted at all by the aerosol route, either in nature or in the laboratory.

Other routes of transmission must also be considered. Splashes and splatters could come in contact with the mucous membranes of eyes, nose, and mouth, or open cuts and wounds. Contamination of laboratory surfaces can contaminate hands, which in turn can lead to infection by mucocutaneous contact or ingestion. Contaminated sharps, such as broken glass, scalpels, and needles, could transmit an agent parenterally. Eating, drinking, or smoking in the laboratory could lead to inadvertent ingestion of an agent.

**Susceptible Route**

To infect a laboratory worker the agent must be transmitted from the animal or insect source or the laboratory sample in a form that can gain entry to the worker by a susceptible route. The susceptible route is dependent on the infecting agent. Some infectious agents may be transmitted by multiple routes whereas others may be restricted to one or two routes. *Plasmodium vivax*, one of the causative agents of malaria, is a bloodborne pathogen and can only be transmitted by the parenteral route through mosquito bites, needles, or sharps. Some enteric pathogens such as *Salmonella typhi* are naturally transmitted by ingestion but could
be transmitted parenterally in the laboratory by sharps. Many of the arboviruses, such as VEE, which require an insect vector for parenteral transmission in nature, may nevertheless be accidentally transmitted in the laboratory by aerosols generated from lab operations.

Unless otherwise carefully documented, it is best to assume that agents can be transmitted by multiple routes.

**Susceptible Host**

Although an agent may gain access to the body through the appropriate portal of entry the host must also be susceptible. Susceptibility to an agent depends on a number of factors ranging from the age of the host, current health, to the immune status of the host. A laboratory worker in good health will generally be more resistant to an infectious disease, and if infected will recover more quickly. Young children, the elderly and those workers with chronic diseases are at higher risk of acquiring infectious diseases. Workers suffering from immunosuppressive diseases or who are treated with immunosuppressive drugs are also at increased risk of acquiring infections in the laboratory and suffering a more severe form of disease than the nonimmunosuppressed person.

**Prophylaxis**

The availability of effective prophylactic measures reduces the worker's risk of acquiring a laboratory infection. The most effective way to reduce susceptibility to an agent is through vaccination. Unfortunately, vaccines are available for only 20 or so of the hundreds of infectious diseases. When available they must be offered to the laboratory worker. However, the limitations of vaccines also need to be understood. Immunity after vaccination declines over a period of time, necessitating a surveillance program that includes periodic revaccinations. Some vaccines require multiple doses over a period of months to stimulate an immune response, and immunity after the first few doses may not be complete. Vaccines such as the influenza vaccines are highly specific for the vaccination strain and may not protect against recent epidemic strains imported from distant outbreaks.

In some cases, such as potential exposures to Hepatitis B virus, it is also possible to boost the resistance of the host by administering specific immune serum globulin. Antibiotics and antivirals also have the potential for being used for prophylactic purposes, although this is rare. During the recent avian influenza outbreak in China, laboratory workers in the U.S. working on clinical samples of influenza isolates from the outbreak in China were offered the anti-influenza agent Rimantidine for additional protection.

**Treatment**

The availability of effective treatment after an exposure reduces the risk to the worker. Specific immune serum immunoglobulin can be given to provide immediate protection to a worker for an exposure to HBV while concurrently vaccinating the worker. Antibiotics are available for most bacterial, rickettsial, and fungal agents, anti-viral chemotherapeutic agents for selected viral agents, and chemotherapeutic agents for many protozoan and parasitic diseases. Generally, treatment is most effective if given as soon as possible after the exposure to the infectious agent to minimize its replicability and to buy time for the immune response to develop. Zidovudine, for example, optimally should be given within several hours after exposure to HIV (CDC, 1998).

**Skill Level**

The degree of knowledge and experience in working with the agent in the laboratory environment and the amount of biological safety training and experience with specific safety work practices influence the level of risk. A knowledgeable and well trained laboratory worker is at a much lower risk of contracting a laboratory-acquired infection than one who isn’t. As the BMBL emphasizes, the higher the biosafety level of the agent, the higher the required skill and experience level of the worker and supervisor.

**Recombinant DNA Microorganisms and Products**

The ability to excise one or more genes from one source of animal, plant, or microbial DNA and to transfer the excised genes into another living organism,
while offering many possibilities of benefiting mankind also offers the possibility of creating new biohazards. One type of biohazard involves transferring gene coding for such characteristics as antibiotic or antiviral resistance, virulence factors, or toxins to other microorganisms, thus increasing their virulence. Other transferred genes may alter the host range, cell tropism, or cell cycle. Another possibility is that nonharmful genes in one host may inadvertently become harmful when transferred to another host. The growing use of viral vectors to introduce genetic elements into plants, animals, and humans also offers possibilities of unforeseen biological hazards. Risk assessments for such potential biological hazards must be reviewed by an Institutional Biological Safety Committee as indicated in the National Institutes of Health Guidelines for Research Involving Recombinant DNA Molecules (USDHHS, 1994).

Risk Assessment and the Biological Safety Program

The risk assessment process is an essential part of an effective biological safety program. The laboratory worker should be knowledgeable about every risk factor for the biological agents commonly used or encountered in the laboratory. Information for these risk assessments is best contained in a biological safety manual. Evaluation of each risk factor for an agent should lead to a risk management procedure. For example, for agents that are transmissible by the aerosol route, every effort should be made to minimize the generation and release of aerosols by using procedures such as using plastic containers instead of (breakable) glass, putting safety cups on centrifuges, confining work with the agent to biosafety cabinets, and using facilities with single passage directional air flow.

Summary

The BMBL provides agent summary statements for more than 100 agents. These agent summary statements provide much of the necessary information for evaluating essential risk factors. However, new and emerging and reemerging agents are continually being encountered. Mahy (1997) has described 40 new viral and rickettsial agents since 1988. Many of these remain poorly described and characterized. Other agents may have developed resistance to antibiotics and chemotherapeutic agents. The host range of many agents, such as Nipah virus and bat lyssaviruses, are not fully known. Genetic engineering offers the possibility of modifying many agents by adding or deleting genes that may further modify the pathogenicity of the agent and create new biohazards or using r-DNA vectors to insert genes into host cell DNAs either in vitro or in vivo. It is these new and emerging agents, for which information is often scarce, for which the risk assessment process is most valuable and the use of the risk factors described herein will hopefully find use in ensuring safe work with these agents in the workplace.

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Laboratory-acquired Human Glanders—Maryland, May 2000

*Morbidity and Mortality Weekly Reports (MMWR)*

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On May 5, 2000, the Baltimore City Health Department was notified by hospital infection-control staff of a serious systemic febrile illness in a microbiologist whose research at the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) involved several pathogenic bacteria, including *Burkholderia mallei*, the causative agent of glanders. This report summarizes the first human case of glanders in the United States since 1945, and emphasizes the importance of considering occupational exposures among laboratory workers with a febrile illness, the difficulty of characterizing unusual agents, including potential agents of biological terrorism such as glanders using routine laboratory techniques, the appropriate isolation practices for patients who may be infected by these agents, and laboratory safety.

The microbiologist, who has insulin-requiring diabetes mellitus, was well until early March 2000, when he developed an increasingly painful mass in his left axilla. On March 16, he had a temperature of 101.5°F (38.6°C) and was seen by a primary-care provider. He was given one dose of ceftriaxone intramuscularly and was started on a 10-day course of cephalexin. Despite completing the therapy, episodes of fever increased, and he experienced marked fatigue, malaise, night sweats, and weight loss. A medical evaluation, which included blood and urine cultures and chest radiographs, was unrevealing. In early April, the patient started a 10-day course of clarithromycin, which improved the symptoms and coincided with resolution of the left axillary mass; however, four days after completing the regimen, his symptoms returned. He continued to lose weight and began to experience mid-epigastric abdominal pain. Multiple blood cultures were obtained and were negative for bacteria.

An abdominal computerized tomography (CT) scan performed on May 2 revealed multiple hepatic and splenic lesions consistent with abscesses. Because of increased abdominal pain, hyperglycemia, and diabetic ketoacidosis, the patient was admitted to hospital A. An ultrasound-guided fine needle aspiration of a medial left hepatic lobe lesion was performed and yielded purulent-appearing material. Blood cultures again were obtained. Because of the patient’s work history, occupationally acquired *Burkholderia mallei* infection was considered, and one dose of piperacillin-tazobactam was administered intravenously. On the second hospital day, the patient developed respiratory distress requiring mechanical ventilatory support. He was placed in respiratory isolation, given intravenous tobramycin and doxycycline, and transferred to hospital B for further treatment.

At the time of transfer on May 4, hospital A identified small, bipolar, weakly-staining Gram-negative rods in cultures of the liver abscess fluid. On May 5, Gram-negative bacteria also were isolated from the blood cultures. An automated bacterial detection system at hospital A initially identified the bacteria as *Pseudomonas fluorescens/putida*. However, subsequent studies of the same isolate performed at hospital B and CDC, including motility studies, cellular fatty acid analyses, and 16S ribosome sequencing, identified the organism isolated from the liver abscess as *B. mallei*.

Because the patient worked with strains of *B. mallei* sensitive to imipenem and doxycycline, he was treated with those antibiotics and his symptoms rapidly improved. Repeat abdominal CT obtained after 10 days of therapy showed slight regression of the hepatic and
splenic abscesses. The patient was treated with intravenous imipenem and doxycycline therapy for two weeks. When he was switched to oral doxycycline and azithromycin, the patient’s liver and spleen abscesses continued to resolve.

The patient reported no exposures to horses, mules, or donkeys. He neither reported nor recalled any laboratory mishaps, although on occasion he had handled without wearing gloves laboratory equipment containing live *Burkholderia* strains. No other persons with whom he lived or worked reported recent febrile illnesses. No health-care workers who came in contact with him while he was a patient have reported symptoms consistent with glanders.

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**Editorial Note**

Glanders is a bacterial infection caused by the Gram-negative rod, *B. mallei* (formerly *Pseudomonas mallei*). Primarily a disease of equids (e.g., horses, mules, and donkeys), glanders also has been reported in carnivores that have fed on infected horse carcasses and, although rare, glanders has been reported in humans. The disease was eliminated from domestic animals in the United States during the 1940s (1) and the last reported human case in the United States occurred in 1945 (2). Glanders still occurs occasionally in equids and humans in central and southeast Asia, the Middle East, parts of Africa, and possibly South America, and *B. mallei* is being researched in the United States because it is considered a potential agent of biological terrorism (3).

In humans, glanders usually is acquired through direct skin or mucous membrane contact with infected animal tissues. The incubation period usually is one to 14 days. The clinical presentation varies (4, 5); cutaneous inoculation can result in localized infection with nodule formation and lymphadenitis (4). The disease often manifests as pneumonia, bronchopneumonia, or lobar pneumonia, with or without bacteremia (4). As in this case, hepatic and splenic involvement has been reported (2). A few antibiotics have been used to treat humans. Sulfadiazine (25 mg/kg intravenously, four times a day) was efficacious in some cases (2). In mice, doxycycline and ciprofloxacin have been effective therapies (6; W. R. Byrne, USAMRIID, personal communication, 2000). The mortality of apparent infection was approximately 95% before the use of antimicrobial agents; however, except when bacteremia develops, better diagnosis and more appropriate therapy have lowered mortality (5). No vaccine against *B. mallei* infection is available.

Glanders has been reported as a laboratory-acquired infection. During World War II, six unrelated cases of laboratory-acquired infection with *B. mallei* occurred at Camp Detrick, Frederick, Maryland (3). Some of these cases were attributed to inhalation of infectious aerosols generated by spillages of liquid culture media containing the bacterium. Other cases were reported to have no obvious cause other than the routine handling of the organism. In this report, the patient did not recall an unusual incident while working with *B. mallei*; however, the presentation of unilateral lymphadenopathy suggests a cutaneous inoculation. Most laboratory-acquired infections are associated with routine handling of microbes and not with injuries (7).

This case raises issues concerning the ability of clinical laboratories to identify rare agents like *B. mallei* rapidly and accurately and the importance of considering occupational exposures among laboratory workers presenting with febrile illness. Serologic and DNA-based diagnostic assays are not standardized, widely available, or approved by the Food and Drug Administration. Automated bacterial identification systems used by most clinical laboratories may not cor-
rectly speciate *B. mallei*, as occurred in this reported case. Effective communication between clinic and laboratory is essential in cases such as this so that unusual pathogens may be considered in the laboratory diagnosis.

Standard precautions (8) (i.e., the use of disposable surgical masks, face shields, and gowns, when appropriate, to prevent splashing of mucous membranes and skin) are sufficient to prevent transmission of this disease to those caring for patients, and biosafety level three is recommended for laboratory staff handling *B. mallei* (9).

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Foot-and-Mouth Disease: A Brief Review of the Etiologic Agent and the Disease Which It Causes

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Abstract

Foot-and-Mouth Disease Virus (FMDV) is the etiologic agent of Foot-and-Mouth Disease (FMD), which is a disease of cattle, swine, and other cloven-footed animals. FMD is characterized by the formation of vesicles on the tongue, nose, muzzle, and coronary bands of infected animals. The virus has several unique characteristics that enable it to cause one of the most economically devastating diseases in today's world. The ease by which it may be transmitted by contact and aerosol, combined with its enhanced ability to initiate infections, virtually ensures that most, if not all, animals in a herd will contract FMD. The long-term survival of FMDV in infected animals' tissues and organs, especially when refrigerated, offers an opportunity for its national and international transmission through the food chain. Multiple serotypes and numerous subtypes reduce the effectiveness and reliability of vaccines. The possible development of carriers in vaccinated animals and those that have recovered from FMD provide additional potential sources of new outbreaks. These features create a disease which can have a major economic impact on farmers and entire nations.

Introduction

As the recent outbreak in the United Kingdom and several countries in Western Europe have demonstrated, FMDV is probably the most feared livestock pathogen in the world because of its devastating effect on cattle, swine, and other domesticated livestock animals which serve as economic pillars of many nations. The unique nature of the virus provides inherent difficulties in its control and eradication. FMDV can be easily and rapidly transmitted by aerosol and direct contact from animal to animal, as well as through mechanical transfer from contaminated environmental materials such as soil and feed. In addition, indirect contact with meat, milk, and hides from infected animals can further spread FMD. Furthermore, FMDV's wide host range, multiple serotypes which contribute to less than effective vaccination and physiologic effects on infected animals can cause economic devastation for farmers. The purpose of this communication is to briefly review the salient characteristics which create FMDV's feared reputation.

Viral Characteristics

Foot-and-Mouth Disease is caused by a small icosahedral RNA virus (picomavirus) with a diameter of 23 nm. The virus is classified in the genus Aphthovirus (from the Greek word aptha, meaning vesicles of the mouth) within the family Picornaviridae. Closely related viruses include the rhinoviruses, polio virus, and the coxsackie viruses. The viral capsid, consisting of approximately 69% of the virion mass, is composed of 60 copies each of 4 polypeptides (i.e., Viral Protein (VP)-1, VP-2, VP-3, VP-4). Subtype specific neutralization epitopes have been identified, among the four capsid proteins, primarily within VP-1.
Host Range

The virus can infect most cloven-footed animals including cattle, swine, sheep and goats, wild pigs, wild ruminants, hedgehogs, armadillos, rats, nutria, and grizzly bears. Human beings are not normally susceptible.

Geographical Distribution

At present, FMD does not exist in North America, Central America, Australia, New Zealand, and until recently, in most countries in Western Europe. The disease is enzootic in Africa, Asia, and most of South America.

Clinical Signs

Cattle and swine show clinical symptoms as early as 24 to 48 hours after infection by FMDV. High viral titers can be demonstrated at this time in the sera of infected animals. FMD is characterized by fever, shivering, drooling of saliva, and the formation of blisters or vesicles on the epithelium of the tongue, nose, coronary bands, and teats as a result of the replication of FMDV. The vesicles are packed with virus particles, as many as $10^8$ per ml. Loss of epithelium is most pronounced on the upper dorsal surface of the tongue, and its desquamation leaves a raw red surface that bleeds easily. Most affected animals will recover within 2 weeks of the onset of symptoms. Secondary bacterial infections of desquamated tissues may delay recovery. The mortality rate for mature animals seldom exceeds 5%, but young animals may have mortality rates as high as 50%. The disease varies somewhat with the species of animals but in general is similar to that of cattle and swine.

Serotypes

FMDV is readily neutralized by antibodies in suckling mouse and cell culture assays. These antibodies are considered the major component of the immunologic defense against the virus. Based on cross serum neutralization tests, FMDV may be classified into seven major serotypes (Types A, O, C, Asia 1, SAT 1-3) and 60 or more subtypes.

Vaccines

Inactivated vaccines for each of FMDV’s major serotypes, as well as multivalent vaccines (e.g., to types A, O, and C) are available. However, vaccines to one major serotype do not cross-protect animals against infections caused by any of the other serotypes. In addition, vaccines produced with one subtype of a major serotype of FMDV may not provide complete protection against infections caused by one or more of the other subtypes of the same serotype. Furthermore, currently available vaccines stimulate the production of antibodies indistinguishable from those produced by infected animals in response to live virus. Thus, vaccination makes it impossible to tell which animals are infected and which are protected. Finally, vaccinated animals may also serve as carriers for several months after being exposed to infected animals. Some countries (e.g., United States, Western Europe) have chosen not to vaccinate because of the cost, logistics of the vaccination process, the carrier state, problems of differentiating vaccinated from infected animals, and reliability problems associated with the vaccines.

Transmissibility

One of the outstanding characteristics of FMDV is its transmissibility. The virus has the unique characteristic of replicating in the nasopharynx and epithelium of the tongue, nose, muzzle, and coronary bands of livestock animals. The coronary bands are located at the junction of the hoofs and skin of livestock animals. It is the replication of FMDV at these sites that leads to the name of the disease, Foot-and-Mouth Disease.

Replication of the virus in the epithelium at these sites causes the formation of blisters or vesicles which are packed with FMDV particles. As the blisters erode, vesicular fluid containing high concentrations of viral particles contaminates the local environment including soil, and grass. Humans may serve as passive vectors of transmission by carrying the virus on their clothes, shoes, tools, etc., to distant locations.

Infected animals can also transmit FMDV by exhaling virus particles from their lungs and nasopharynx into the atmosphere. Swine are particularly potent amplifiers of the virus and can release huge amounts of
Foot-and-Mouth Disease

virus into the atmosphere through exhaled air. Under appropriate conditions, FMDV can be carried considerable distances by the winds to infect additional animals. The 1981 FMD outbreak in the United Kingdom, which occurred on the Isle of Wight in the English Channel, is believed to have resulted from the airborne spread of the virus from Brittany in Northern France. Because of the high transmissibility of FMD by both the aerosol and contact routes, it is likely that if one bovine or swine in a herd is infected, most, if not all, other animals will be infected within a relatively short period of time.

FMDV may persist in tissues of dead animals for considerable periods of time (e.g., upwards of several months in the refrigerated internal organs, green unsalted hides, bone marrow, lymph nodes, and residual blood). Any product or by-product of infected animals can contain viable viral particles capable of infecting livestock in the country of origin or in countries which have imported these products. In 1967, the spread of FMDV in England resulted from the consumption of infected meat scraps by pigs. It is likely that the current outbreak of FMD in the United Kingdom originated in a similar fashion.

The Carrier State

Cattle, and perhaps other susceptible animals, that have recovered from FMD may carry the viable viral particles in their esophageal-pharyngeal fluid for 4 to 24 months post infection. Vaccinated animals exposed to FMDV have also been shown to be able to serve as carriers. Although vaccination does not prevent the carrier state, it does appear to reduce the spread of the virus among cattle. Laboratory studies have not documented the transmission of FMDV from carrier to susceptible animals, but carriers nevertheless remain a potential vehicle for transmission under field conditions.

Economic Consequences

As the vesicles on the tongue erode, it becomes painful for the infected animal to eat or drink and the animal begins to salivate excessively. Similarly, erosion of the vesicles on the feet makes it difficult for animals to walk as they begin to demonstrate lameness. Thus, infected cattle may lose up to 30% of their body weight in a week or two because of difficulty eating, drinking, and walking to food. In dairy cattle, vesicular lesions can also occur on the teats and udder, sometimes leading to secondary bacterial mastitis.

While the vesicles heal in a week or two, the severe loss in body weight of meat cattle can become an economic disaster as the farmer's profit margins are dependent upon the weight of the animals when presented at market. In addition, dairy farmers may also suffer a significant economic impact through decreased milk production of infected animals.

Laboratory Containment

Laboratory work with FMDV in the United States is restricted by law to an island separate from the mainland. Since 1954, work with FMDV, as well as a number of other exotic animal disease agents, has been confined to the United States Department of Agriculture's Plum Island Animal Disease Center (PIADC), located off the eastern tip of Long Island, New York. At PIADC all work is carried out in enhanced BSL-3 laboratory and animal facilities. Enhancements include passage of exhaust air through HEPA filters, heat inactivation of all liquid wastes, incineration of animal tissues and carcasses, and decontamination of all other materials leaving the containment facilities by steam under pressure, ethylene oxide, formaldehyde gas, and other suitable disinfectants. Further enhancements include mandatory change clothes in/shower out requirements for all personnel and mandatory quarantine of all personnel and visitors from contact with cloven-footed animals for seven days after leaving the island.

Conclusion

Because of the high transmissibility of FMDV from both animals and animal products, disease-free countries will not import animals or their products from countries undergoing an outbreak for at least 6 months after the termination of the outbreak. The economic consequences of these actions could well be the loss of hundreds of millions, perhaps billions, of dollars in revenues for the exporting nation. The national programs which must be instituted to control the transmis-
sion of FMDV (e.g., destruction of herds in which there is even one infected animal, disinfection and quarantine of farm premises, and implementation of import restrictions by other nations for animals and animal products from the affected nation) will further impact the outbreak nation's economy. Finally, there is the compensation that must be paid to affected farmers. The recent outbreak in the United Kingdom serves to remind us of the fearsome nature of the virus and the disease which it causes.

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Capsule

Ed Krisiunas

WNWN International, Burlington, Connecticut

The Capsule section of Special Features was designed to provide timely information on "what's hot in the news—what's happening of note." It is our intention to provide readers with snippets on noteworthy events and information, along with the references needed to further investigate the subject. We hope the section will be of assistance and encourage you to contact us with topics you feel would be of interest to our readers.

Foot-and-Mouth Disease (FMD)

Foot and Mouth Disease has wreaked havoc in Europe since the late winter. Heightened concerns have led the U.S. Department of Agriculture (USDA) to increase its efforts to prevent the entry of this disease into the U.S., last seen here in 1929.

David Huxsoll, director of the Agriculture Department's Plum Island Laboratory off Long Island, New York, recently indicated that chances of an outbreak are "quite great," considering the amount of people that travel between the United States and Britain."

USDA has established a coordinated effort with other departments including the departments of Defense and Interior as well as the Federal Emergency Management Agency (FEMA) to ensure adequate resources are available to address an outbreak. For more information and resources on FMD, see:

www.usda.gov/

Bovine Spongiform Encephalopathy (BSE)

FMD is not the only serious concern to regulators, industry, and the public. Bovine Spongiform Encephalo-

opathy (BSE), better known as Mad Cow Disease is also of concern. The FDA published a report on BSE on March 1, 2001 that deals with the background, current concerns, and the U.S. response. It can be viewed and downloaded from:

www.fda.gov/opacom/backgrounders/bse.html

West Nile Virus


The revised “Guidelines for Surveillance, Prevention, and Control of West Nile Virus Infection—United States, 2001” are now available from CDC at: www.cdc.gov/ncidod/dvbid/westnile/publications.htm

The revision of the 2000 Guidelines (CDC, 2000) was derived from discussions during the national meeting on West Nile virus held in Charlotte, North Carolina, during January 31 - February 4, 2001 (Gubler, Campbell, Petersen, & Roehrig, 2000).

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Biosafety and Genetically Modified Organisms

Biosafety professionals are beginning to realize the application of biosafety goes well beyond the laboratory, whether it be in a clinical or research setting. New issues and frontiers exist that we would not have imagined 30 years ago. Addressing the issues of Genetically Modified Organisms (GMOs) is one of those challenges. As we have seen with FMD and BSE, organisms can have great economic as well as political impact. The Third World Network (TWN) has a web site that addresses issues faced by developing countries as GMOs and products are introduced into the world market. A draft “Biosafety Protocol” is presented which discusses several aspects that countries could consider as they venture into the arena of GMOs. For more information, see:

www.twinside.org.sg/bio.htm

OSHA Needlestick Requirements Take Effect April 18

OSHA announced on April 12 that changes in its bloodborne pathogens standard intended to reduce needlesticks among health care workers and others who handle medical sharps went into effect April 18, 2001. The agency instituted a 90-day outreach and education effort before enforcing the new rules.

Mandated by the Needlestick Safety and Prevention Act, changes to OSHA’s bloodborne pathogens standard were published January 18, 2001, to take effect April 18, 2001. The revisions clarify the need for employers to select safer needle devices as they become available and to invoice employees in identifying and choosing the devices. The updated standard also requires employers to maintain a log of injuries from contaminated sharps.

The legislation exempted OSHA from certain standard rulemaking requirements so that the revised bloodborne pathogens standard could be adopted quickly. These changes now go into effect as originally scheduled. For more information, see:

www.osha.gov
Ask the Experts

John H. Keene

Biohaztec Associates, Inc., Midlothian, Virginia

This is the first of what we hope will be a continuing forum for ABSA members to obtain answers to questions that are of particular interest to professionals in Biosafety. We encourage you to send us questions that concern you and that you feel may be of interest to others in the profession. We will attempt to get expert advice on these topics and publish them in this column in each issue of Applied Biosafety: Journal of the American Biological Safety Association. We hope to have several pertinent questions and their answers in each issue. The success of this endeavor will be up to you, the membership. Please help yourself, your organization, and your fellow biosafety professionals by submitting your questions for publication.

Question:

IATA USG 12 (International Air Transport Association Dangerous Goods Regulations Section 2 [Limitations] United States Government limitation 12; page 35 IATA Dangerous Goods Regulations) refers to a 24-hour emergency response telephone number required on Shipper’s Declarations of Dangerous Goods. In our shipping training, we teach that this 24-hour number be exactly as dictated in the regulations. We get questioned on this by people who insist the CDC supplies this number. We know that the number published by CDC on the Class 6.2 label is for reporting an accident and NOT for the 24-hour emergency response. Are we correct in this stance or have we been wrong all along? If we are correct, is there some way we can get a statement from CDC explaining this? Any light you might shed on this question would be greatly appreciated.

Answer:
(From Richard Knudsen, CDC)

The 24-hour emergency response telephone number listed in the IATA DG (International Air Transport Association Dangerous Goods Regulations) should be the shipper’s emergency number. The purpose of this number is to provide 24-hour emergency access to information about the contents of the package, should there be damage to the package and potential exposure. It is completely inappropriate to use CDC’s telephone number for this purpose. The CDC number should be used only to notify CDC of a damaged package, or, in the case of a special etiologic agent, to report a package that has not arrived within the specified timeframe. CDC also provides advice on how to handle the damaged package and often advises the handler that, since CDC does not know the contents of the package, he or she should call the 24-hour emergency response number to determine the contents and then to refer back to CDC for further advice. The use of the CDC number as a shipper’s emergency response number may be considered a violation of the FAA regulations and result in stiff civil or criminal penalties.

Question:

We are involved with CDC as a regional resource under their Bio-Terrorism (BT) initiative. As such, we are required to use a “Taq-man” to identify BT agents such as “Anthrax.” As you probably know, these instruments are very expensive. We are in the process of buying such an instrument and are debating where it should be located—in the BSL-3 BT suite, or in a BSL-2 suite where it would be available for not only
BT samples but also other non BT samples. My question is “Would it be safe to prep a potential Anthrax BT sample in the BSL-3 suite and then transfer the genetic material to the Taq-man located in a non BSL-3 suite on another floor?”

**Answer:**
*(From Richard Knudsen, CDC)*

All work with infectious agents at BSL-3 should be done in a biosafety cabinet (BSC). Extract the DNA from your sample with lysing buffer in a closed tube in the BSC; the lysing buffer should inactivate the agent. You can then decontaminate the outside of the tube and transfer it to your BSL-2 lab for taq-man analysis. The only possible danger is spores surviving the lysing buffer. I suggest that the investigator test the lysing buffer for effectiveness in destroying the spores. If one lysing buffer doesn't inactivate the spores, you may want to test one of several others. In any case, the limiting factor is the survivability of the agent after treatment with the lysing buffer. If you can't eliminate the spores one way or another, this would probably require that the taq-man work be done at BSL-3. We have used a similar procedure to remove DNA extracted from BSL-4 agents from the BSL-4 lab after the investigator provided test data to verify that the agent did not survive the lysing buffer.
Regulatory Affairs

Ira F. Salkin
New York State Department of Health, Albany, New York

Two recent developments are designed to improve the safety of health care workers. The first is federal legislation recently passed by the United States Congress and signed into law by President Clinton. The Needlestick Safety and Prevention Act was initially introduced into the House of Representatives (HR 5178) by Cass Ballenger (Republican from North Carolina) and Major Owens (Democrat from New York). A companion bill which mirrored the House legislation was introduced in the Senate (S 3067) by James Jeffords (Republican from Vermont). The Act modifies the current Occupational Safety and Health Administration’s (OSHA) bloodborne pathogens standards to require employers to consider and implement the use of “safer medical devices.” These devices are described in the law as needles and other medical equipment designed to reduce or eliminate percutaneous injuries of health care workers and thereby decrease the employees’ exposure to bloodborne pathogens. In addition, the law requires health care facilities:

• To document and maintain a log of needlestick incidents of all employees
• To identify, evaluate, and introduce the use of safer devices
• To solicit employee input regarding the evaluation and selection of the devices
• To introduce improved training and education programs to familiarize employees with the new legislation, the use of the safer medical devices selected for use within the facilities, and the dangers associated with needlestick injuries and bloodborne pathogens

The Secretary of Labor is required to publish a notice of the new law in the Federal Register within 6 months of its enactment (December, 2000) and is afforded an additional 3 months to modify OSHA’s current bloodborne standards to incorporate these new regulations pertaining to the use of the safer medical devices. Therefore, it is possible that the health care industry in the United States could see the new requirements as early as August, 2001.

The second development includes proposed new regulations designed to reduce potential Hepatitis C (HCV) contamination of the United States blood supply. These new rules were published by the Food & Drug Administration (FDA) and the Health Care Financing Administration (HCFA) in the Federal Register on November 16, 2000 (search phrase = Current Good Manufacturing Practices for Blood and Blood Products). The FDA regulations will require all facilities involved in the collection, processing, testing, and administration of blood units (e.g., health care institutions, free-standing blood banks, and plasma facilities) to develop and introduce procedures to ensure the public’s safety when blood and blood components are reasonably presumed to contain HCV. Specifically, the facilities will have to quarantine blood and blood components collected from a donor who has been found upon repeated testing to be HCV-positive. In addition, these same health care institutions must make at least three attempts to notify transfusion recipients within 1 year when the HCV-positive status of a donor is discovered at repeat donation. Furthermore, the facilities must inform recipients if an evaluation of its records indicates potential HCV-contaminated units from the donor were used to transfuse patients.

The HCFA proposal would require free-standing blood banks to notify hospitals when they have supplied potentially HCV-contaminated blood and blood products. As in the FDA proposed regulations, the hospitals in turn must quarantine all blood units received from such HCV-infected donors, conduct searches of
their records to determine whether donations from these or other HCV-infected individuals have been previously employed in transfusions, and notify the recipients of the donations when repeated tests of the donors indicate HCV infections. The HCFA proposal would be included in its Conditions of Participation under which hospitals receive reimbursement as Medicare/Medicaid providers.

If the proposals are adopted, probably sometime in 2001, facilities which do not meet these requirements will lose FDA’s certification as blood banks and HCFA’s approval to participate in the Medicare/Medicaid programs.

Editor’s note: This article is reprinted from AIDS and Hepatitis Digest, Number 87, March 2001. Reprinted with permission of the Royal Society of Medicine Press.
Innovations—Rapid Assessment of Mold: Contamination on Environmental Surfaces

Eugene C. Cole
DynCorp Health Research Service, Morrisville, North Carolina

A rapid tool for assessing levels of total fungal contamination on surfaces has been developed and patented by scientists at the University of Copenhagen. This MycoMeter-Test is based on the fluorometric detection of N-acetylhexosaminidase and is extremely specific for fungal contamination, with cross-reactivity from bacteria practically zero, and few false-positive materials. Using sterile cotton swabs for sample collection, the portable test kit comes with all required components, including disposable templates for standardization of samples, all necessary reagents, and a photometer for reading results. Incubation time is only 30 minutes, allowing rapid onsite evaluation. Existing research data show that assessment results can fall into one of three levels: Level A (mold levels are not above normal background levels); Level B (mold levels are above background levels due to presence of spores and/or old mold growth); and Level C (mold levels are above background levels due to active fungal growth). Levels equate with defined numerical value ranges.

The rapidness of the test makes it an extremely desirable diagnostic tool where decisions need to be made quickly, without the typical wait of several days to a week or more for traditional culture techniques. I have seen the MycoMeter-Test used to evaluate a variety of different surfaces and materials, and find it can easily be incorporated into a customized program of contamination control. For example, it can be used to measure acceptability of surface cleanliness in a wide variety of applications, such as assessment of sanitization procedures before, after, and relative to mold remediation of a water-damaged building, validation of a cleanroom production facility, decontamination of a biohazard containment laboratory or bone marrow transplant unit, and many others.

The MycoMeter-Test was presented at Healthy Buildings 2000 in Finland, and a brief paper has been published in the conference proceedings (Proceedings of Healthy Buildings 2000, Vol. 1, pp. 589-590). While the MycoMeter-Test is currently available from Mycotec, Copenhagen, Denmark (www.mycotec.dk), additional applied research is planned for the United States to further fine-tune the technology. An eventual system of American distributors is also planned. And while the current cost of an individual test is approximately the same as for a fungal culture, I would expect that cost to decrease as the product becomes more widely utilized and production volume increases. In summary, I view this as an exciting and innovative product to be utilized in a multitude of biological contamination control programs and related applications. I look forward to reviewing additional field performance data on the MycoMeter-Test in the near future, and bringing you an updated report.
New Publications

Mary Ann Sondrini
Eagleson Institute, Sanford, Maine

**Biological Safety: Principles and Practices, 3rd Edition**

ASM Press recently published the third edition of *Biological Safety: Principles and Practices*. This 784-page comprehensive book contains 39 chapters, divided into sections on Hazard Identification, Hazard Assessment, Hazard Control, Administrative Controls, and Special Considerations for Biosafety. Detailed chapters cover the epidemiology of laboratory-associated infections as well as hazard assessments of the wide range of pathogens and biological toxins encountered in biomedical laboratories. All facets of hazard control are discussed. Editors are Diane O. Fleming, PhD, and Debra L. Hunt, DrPH.

Order this book from ASM Press at 1-800-546-2416 or www.asmpress.org. Cost is $89.95.

**Primary Containment for Biohazards: Selection, Installation and Use of Biological Safety Cabinets, 2nd Edition**

The pink book is now the green book. CDC recently published the second edition of this companion to the BMBL. This booklet provides an overview of Biological Safety Cabinets, with chapters on the different types of cabinets, the use of hazards in the cabinet, effective work practices and procedures, facility and engineering requirements, and certification of cabinets.

To receive a free copy, e-mail Audrey Anderson at aha2@cdc.gov.

**6th National Symposium on Biosafety Proceedings: Prudent Practices for the New Millennium**

These proceedings are from the symposium held February 6-9, 2000 in Atlanta, Georgia. Many of the speaker presentations are included in the proceedings. Topics range from emerging infectious diseases, risk management, safety issues when working and transporting animals, and bioterrorism, to issues in communication.

These proceedings can be purchased from ABSA. The cost is $26.00 for members and $39.00 for nonmembers.
The Training Exchange—The Importance of Understanding Communication Styles When Teaching

Mary Ann Sondrini
Eagleson Institute, Sanford, Maine

Do you sometimes wonder why it is so difficult to communicate with some people and so easy with others? When you offer training classes, do you find some classes more receptive than others? What accounts for these differences?

I like to think of communication as a speaker, a listener, and a piece of Swiss cheese in between. What we say goes in one hole and out another, passing through a series of filters. These filters might include perceptions, assumptions, knowledge differences, distractions, preconceived notions, or perhaps different communication styles, which is the topic of this article.

Carl Yung, a Swiss psychoanalyst, developed the idea that behavioral patterns fall into four major categories. Psychologist Paul Mok translated Jung's theories into four communication styles, which explain how people process and send messages. If you would like someone to understand what you are saying to them, you need to speak to them in their preferred style of communicating, not your own preferred style. If you are teaching a class or giving a presentation, you need to consider techniques for reaching all four behavioral groups.

What are these four styles? The first one is called intuitor. Intuitors place a heavy emphasis on ideas and long-range thinking. They have vision, are imaginative, focus on the future, and have the ability to see relationships that many others do not understand. They tend to ask many questions so that they can fit all the pieces together.

A second style is called thinker, which is characterized by a heavy emphasis on logic. Thinkers find it satisfying to identify a problem, develop a variety of solutions, weigh them carefully, and test them to see that the most logical, systematic approach is followed. They avoid emotionalism and speculation.

Feelers, the third style, focus on interactions with other people. They seek to understand and analyze their emotions and those of others, and are astute at reading between the lines. They tend to be sensitive to the needs of others, and are often seen as very dynamic and emotional.

The fourth style is sensor, which is characterized by action. Sensors get things done. They are direct, down-to-earth, and energetic, learning best by personal experience. They are only interested in ideas that are practical and workable.

When developing a training program, you must think about all four communication styles explained above. How are you reaching the intuitor? Are you including information on the long-term value of your program? What about the thinker? Are you showing data to support your ideas? To reach the feelers in the group, you may want to share personal stories related to your topic. As for the sensors, make it clear that you are not wasting their time and that they will derive immediate benefits from the program.

If you would like to take a survey to learn what your preferred style is, or would like more information on this topic, contact Training Associates Press (www.tapress.com).

Author's note: For the next Training Exchange article, I'd like to focus on ideas for bloodborne pathogen training. Please submit some of your training ideas to share with other ABSA members by sending me an e-mail at maryann@eagleson.org. I will be sure to give you credit. Thank you.
Using the Web—Using the Web to Write or Modify a Biosafety Manual (BSM)

Richard C. Fink
Massachusetts Institute of Technology, Cambridge, Massachusetts

This is a new column for Applied Biosafety: Journal of the American Biological Safety Association. In it, I will try to highlight web sites of interest to biosafety professionals as well as how to search the Web to answer questions that come floating over the e-mail list, Biosafety. This first column relates to e-mail questions.

One of the frequent requests on the e-mail list Biosafety is how to either write a biosafety manual or write a particular section within the manual. The WWW is a great place to start on that quest. Using the search terms (biosafety OR [biological safety]) NEAR manual, on Northern Light (northernlight.com) yielded 18,997 hits. What follows is not a detailed description of each and every site but a synopsis of what can be found.

The first 17 hits are from various universities in the United States, Canada, and Australia. By adding additional terms in your search, you can narrow the search down to a particular country or biosafety level. For example, changing the above search to read (biosafety OR [biological safety]) NEAR (manual and [BL3 OR BSL3 OR “BL 3” OR “BSL 3”]), one gets only 88 hits. Thus, by carefully selecting your search parameters, you can narrow your search to a manageable size.

Another way is to go to the web site of a university that is similar to yours to see if they have their manual on-line. A great web site is www.mit.edu:8001/people/cdemello/univ.html, which is a site of links to college and university web sites around the world. Most biotechnology industries do not post their manuals on their public site, but a university’s BSM could easily be adapted for industrial use, especially one written with large-scale procedures in place.

Note: Web search services are not equal. An article in Nature about a year ago gave Northern Light a slight edge over Alta Vista in the number of web pages indexed. Both of these search services far exceed in sites indexed the other popular search services available. An interesting search service is Ask Jeeves (www.askjeeves.com/) which allows one to ask a question, such as “What is the biosafety level of a transgenic mouse?” This question returned 50 hits, all involved with biotechnology, and mainly transgene (both animal and crop). The most interesting site found was “Transgenic Mouse Core Facility Purdue University Transgenic Mouse Core Facility Instruction Manual for Users.” This didn’t cover biosafety, but was interesting nevertheless.
Position Paper—HIV Prevention

Debra L. Hunt
Duke University Medical Center, Durham, North Carolina

HIV Prevention Plan Comments
National Center for HIV, STP, and TB Prevention
Centers for Disease Control and Prevention
1600 Clifton Road, NE
Atlanta, GA 30333

February 5, 2001

Dear Sirs,

The American Biological Safety Association (ABSA) is an organization of biological safety practitioners who work in a variety of academic, governmental, and private work environments. We have many members in the United States, Canada, and in other countries. We are recognized as the leading authority in the field of biological safety.

We have reviewed your draft September 2000 HIV Prevention Plan through 2005. Please consider the comments which follow regarding Goal 1, Objective 11; “Reduce occupational transmission of HIV.”

The strategy to encourage the availability and use of effective engineering controls with engineered sharps injury protection is to be endorsed. It is consistent with other Centers for Disease Control and Prevention (CDC) recommendations and the bloodborne pathogens compliance directive from the Occupational Safety and Health Administration (OSHA). The need for employees who use sharps to also utilize safe work practices and be trained in the use of the engineered sharps’ injury protection must be stressed. The means of activation and verification of activation of the engineering control must be understood by employees using them. The engineering control must also be properly evaluated by the employer in the work environment in which it is to be used. Some devices may not be able to work comparably in all needle use situations. These work conditions can affect the employee's ability to benefit from the protection of the engineering control.

Disposable gloves are recognized as barriers to bloodborne pathogens. Employers need to be encouraged to select effective barrier protection for use by their employees. Latex is still recognized as the glove material most resistant to bloodborne pathogen penetration. Employers should select powder-free latex gloves with low levels of water-soluble extractable proteins. This is consistent with the recommendations of the National Institutes of Occupational Safety and Health (NIOSH). These gloves should also have been issued 510(k)'s by the Food and Drug Administration (FDA) to verify that they meet medical device requirements. Gloves should also be manufactured as per the applicable American Society of Testing Materials (ASTM) standards. Gloves of alternative, nonlatex materials meeting these requirements need to be made available to employees with latex allergies or other sensitivities to glove materials.

There are many clinical trials underway all over the world involving anti-HIV drugs. Care must also be taken when specimens from patients in these trials are sent to the United States for testing. Physicians forwarding these specimens must be educated and take proper care in the preparation of these shipments. This is in keeping with International Civil Aviation Organization/International Air Transport Association requirements. This is needed to help avoid possible HIV transmission to the public.

We agree that health care workers need to be made aware of postexposure prophylaxis. However, all anti-HIV drugs currently recommended in the CDC guidelines are not available in all medical practice situations. Employers should identify medical practices that can
provide comprehensive treatment and arrange for the provision of such medical services prior to employee exposure. Timely counseling and treatment are essential to prevent an exposure from resulting in HIV infection. The employee also needs to be properly prepared to make the necessary personal decisions regarding an acceptable postexposure treatment (i.e., the timely use of AZT, etc.). Insurers need to be encouraged to determine the capabilities of practices in their provider networks to provide comprehensive HIV treatment as per the CDC recommendations. Insurers then need to communicate this information to their clients. These combined efforts would result in better ability of medical practices to render proper treatment and to prevent the development of HIV infection in these exposure situations.

We appreciate the opportunity to have provided this input to your strategic plan. We wish you well in these efforts.

Sincerely,

Debra L. Hunt, DrPH, RBP, CBSP
President, American Biological Safety Association

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**IMPORTANT IMPORTANT IMPORTANT IMPORTANT IMPORTANT**

A change of address notice should be sent at least six weeks in advance to the ABSA National Office to ensure that all mailings, including the journal and newsletter, will reach you. ABSA is not responsible for misrouted mail as a result of insufficient notification of an address change. Undelivered copies resulting from an insufficient address change notification will not be replaced, but single issues may be purchased at the single issue price.

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Position Paper—Arthropod Containment

Debra L. Hunt
Duke University Medical Center, Durham, North Carolina

Dr. Mark Benedict
CDC/NCID/DPD Entomology MS F-22
4770 Buford Highway
Chamblee, GA 30341

February 2001

Dear Dr. Benedict,

The American Biological Safety Association (ABSA) appreciates the opportunity to provide comments on the draft “Arthropod Containment Guidelines” (ACG) of the American Society of Tropical Medicine and Hygiene (ASTMH). It is clear that much considered thought and effort have gone into the preparation of this document. Your group is to be commended for initiating these guidelines. We hope that the input that follows will help to make them even more useful for safety professionals and the research community.

Arthropods Containing Known Infectious Agents

On page 13, the paragraph begins, “Readers will observed that the….” The paragraph should read, “Readers will observe.”

Arthropod Containment Levels

The technical concept of being able to work with an arthropod bearing a class 3 pathogen in a low-risk area can be appreciated. However, consideration should also be given to the possibility of a transmission of such a pathogen from a low-risk area to a high-risk area. The world’s population is uncommonly mobile today. Arthropods in a low-risk area could unknowingly be transmitted to a high-risk area by a national or international air traveler. Such situations are occurring with vectors and animals already. This situation needs consideration when selecting containment for class 3 pathogen-infected arthropods. Greater emphasis should also be placed on steps to protect workers from infected arthropods.

Arthropod Containment Level 1 (ACL-1)

The use of sharps with engineered sharps injury protection is to be endorsed. The statement requiring engineering controls in this level and others is evidence that the authors are proactive and current in recent safety and health developments.

Arthropod Containment Level 2 (ACL-2)

Some guidance on the prevention of viable stages to the drainage system following hand washing would be prudent (e.g., the use of filters or biocidal traps). Clarification on autoclave placement would be helpful. The Biosafety in Microbiological and Biomedical Laboratories (BMBL) indicates that autoclaves must be in the facility, and it provides transport requirements if viable materials need to be moved to the autoclave room for sterilization. Such guidance is not given here. Also, specific recommendations regarding the Heating, Ventilation, and Air Conditioning (HVAC) system are lacking. These details would be useful.
Arthropod Containment Level 3 (ACL-3)

There is a suggestion that containers be autoclavable or disposable. Later, it is recommended that these containers be disposable. It is prudent to autoclave all containers before disposal.

In the section on floor drains, there is consideration for a heat or chemical treatment system. This specific consideration is not detailed for the plumbing or showers to protect arthropod escape. Also, floor drains are not recommended, but showers are required. ACL-2 is referenced for plumbing, but the previous plumbing section discusses effluent treatment systems at ACL-3 which is part of the plumbing system. This needs to be clarified.

A recommendation is made for appropriate filter/barriers to prevent the escape of arthropods. It is unclear if this is in addition to the use of High Efficiency Particulate Air Filter (HEPA) filters. If this is to be done in addition to the use of HEPA filters, then is there an optimal mesh size for the screens?

There is a recommendation that spaces around doors need to be sealed with tape or plastic sheeting. Clarification needs to be provided if that is to be done at all times or only at the times that the facility is being decontaminated.

Arthropod Containment Level 1 (ACL-4)

In the first paragraph there is a passage that reads, "...pathogens often require experimental attempts to infect arthropod..." The passage should read, "arthropods."

General Packaging Requirements for Transport of Live Arthropod Vectors

The definition for select agent is given as etiologic agents listed in 42 Code of Federal Regulations (CFR) 72. The select agent listing is detailed in Appendix A of 42 CFR 72.6 so as not to confuse these agents with the list of etiologic agents. This reference needs to be corrected to be consistent with the Centers for Disease Control and Prevention (CDC) listings.

Table 1: Summary of Arthropod Containment Levels

There could be some changes made that would make this table easier to read and use. Under the heading of Arthropod Containment Level 1-4, each column with a numbering would also indicate ACL-1, ACL-2, ACL-3, ACL-4, or the heading Arthropod Containment Level would be followed by ACL-1, ACL-2, etc. The fates of exotic arthropods are not clear. They are clustered with ACL-2 through ACL-4, but they are also separately listed under ACL-1.

General

There is a comment in these guidelines about vaccines being available for LaCrosse but not for Eastern Equine Encephalitis (EEE). The BMBL indicates that both EEE and Western Equine Encephalitis (WEE) vaccines are still available from the CDC or United States Army Medical Research Institute for Infectious Diseases (USAMRIID). Both vaccines are no longer available since efficacy testing is incomplete. The current and expected availability of these vaccines should be clarified.

Thank you once more for the chance to have provided input for a set of guidelines.

Sincerely,

Debra L. Hunt, DrPH, RBP, CBSP
President, American Biological Safety Association
Position Paper—Recombinant DNA

Debra L. Hunt

Duke University Medical Center, Durham, North Carolina

Office of Biotechnology Activities
National Institutes of Health
Building 1, Room 103
Bethesda, MD 20892

February 2001

Dear Sirs,

The American Biological Safety Association (ABSA) is an organization of biological safety practitioners who work in a variety of academic, government, and private work environments. We have reviewed your Notice of Proposed Action under the National Institute of Health (NIH) Guidelines for Research Involving Recombinant DNA Molecules that was published in the December 12, 2000 issue of the Federal Register. Please consider the comments that follow.

We approve and support the general content and scope of the proposed changes to the guidelines. The refinement of the definition for sudden adverse events (SAEs) and the tightening of the timeframes for reporting them are positive steps for harmonization of NIH and Food and Drug Administration (FDA) SAE requirements that should be endorsed. These efforts will help to prevent SAEs from being considered trade secrets, but they also prevent the inclusion of patient identifiers and other confidential information in the report.

The Office of Biotechnology Activities' (OBA) changes in the review of SAEs are to be applauded. All Institutional Biosafety Committees (IBCs), even ones at large universities with major medical centers, do not always have the needed expertise for the SAE review. Some Institutional Review Boards (IRBs) are better equipped for these reviews, but they don’t always have expertise in gene therapy. The perspective of the OBA will also be of value, since it will have access to SAEs from other institutions. The OBA should warn all clinical sites of a potential problem with a gene therapy protocol before examination by the Gene Transfer Safety Assessment Board.

Local IRBs and IBCs should be party to communications between OBA and principal investigators on human gene therapy research projects. RAC decisions would also need to be communicated to IRBs and IBCs. The Gene Transfer Safety Assessment Board conclusions also would need to be disseminated to these parties in a timely manner.

Adverse event (AE) and SAE report forms should be identical to the FDA’s. A subject identifier is a major benefit of these forms. This enables the Gene Transfer Safety Assessment Board and the public to determine if SAEs are in one or more subjects. NIH may want to consider reformatting its forms to more closely match FDA’s. It is understood that the information collected in each form is destined for different uses.

The identification in applications of all IBCs, IRBs, and the proposed clinical sites that are required in Appendix M of the guidelines does not always occur. Some studies involve multiple clinical investigators at more than one hospital or university. It must be an absolute requirement to identify these investigators and locations in applications.

Despite the improved definitions, some Principal Investigators (PIs) may not recognize that an unexpected SAE is associated with a gene transfer project. The sponsor needs to train the PI, or provide PIs with information related to the gene therapy agent. Reporting as soon as possible or within 7 days of the PI’s receipt of information of the event should be required.
The Gene Transfer Safety Assessment Board Working Group should include an epidemiologist and a pathologist. Inclusion of a molecular biologist/molecular virologist, preferably a basic scientist rather than a clinician, should also be considered. The basic science molecular biologists often bring to the discussion includes less well known aspects of molecular mechanisms associated with gene transfer. The perspective of a biological safety professional is not only beneficial, but ultimately necessary for this Working Group to address all aspects of health and safety. For this reason, an ABSA member who is also a certified biological safety professional (CBSP) should be appointed to this group. ABSA reviews the areas of interest of CBSPs, and determines the willingness to serve of CBSPs with the pertinent expertise. The names of these individuals could be provided to the NIH Director, who would make the appointment.

We appreciate the opportunity to provide input to your proposals.

Sincerely,

Debra L. Hunt, DrPH, RBP, CBSP
President, American Biological Safety Association
Anthology I: Perspectives on Laboratory Design
Contents include, in part: Management of Biosafety; Design Issues at the Management/Facility Interface; Primary Biocontainment Devices; HVAC Issues in Secondary Biocontainment; Open BSL-2 Laboratories; Facility Guidelines for BSL-2 and BSL-3 Biological Laboratories; Design of BSL-3 Laboratories; Building a Maximum Containment Laboratory; Designing the BSL-4 Laboratory; Role of the Class III Cabinet in Achieving BSL-4; Containment Design Concepts for Extraterrestrial Sample Return; Biosafety Considerations for Design of Large Scale Facilities; Small Animal Research Facilities and Equipment; Small Animal Research Facility Management; Large Animal Research Facilities; and Waste Management Considerations.

Anthology II: Facility Design Considerations
Contents include, in part: Working Safely with Wild Poliovirus; Biocontainment of Highly Pathogenic Avian Influenza Viruses; Maximum Containment for Researchers Exposed to Biosafety Level 4 Agents; Modular/Mobile BSL-2/3 Laboratories; Facility Maintenance Operations (Skilled Trades) for Biological Containment Laboratories; Construction and Commissioning Guidelines for Biosafety Level 4 (BSL-4) Facilities; Safety and Health Considerations for Conducting Work with Biological Toxins; Primary Containment Devices for Toxicological Research and Chemical Process Laboratories; Toxicology Laboratories; and Medical and Infectious Waste Management.

Anthology III: Application of Principles
Contents include, in part: Risk Assessment for Working with Infectious Agents in the Biological Laboratory; Biosafety Considerations in rDNA: Viral Gene Transfer Vectors, DNA-based Vaccines and Xenotransplantation; Biological Safety and the Academic Environment; Biosafety Issues in Hospital Settings; An Overview: Biological Safety from a Global Perspective; Beyond Compliance: Global Biological Safety at Johnson & Johnson; Twenty Years of Global Biosafety Programs; Ergonomic Considerations in Biomedical Research Laboratories; and Applied Safety Training in the Biomedical Facility.

ABSA/CDC 5th National Symposium Proceedings: Rational Basis for Biocontainment
Papers presented during the 4-day conference jointly sponsored by ABSA and CDC from January 17-20, 1998 in Atlanta, Georgia.

Papers presented during the 4-day conference jointly sponsored by ABSA and CDC from February 6-9, 2000 in Atlanta, Georgia.

Both of these proceedings provide detailed information for biological safety professionals, architects, engineers, and attorneys in the development, design, and operation of containment laboratories of all sizes. This is a must read for those involved in the operation and/or development of a containment laboratory.

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Guidelines for Submissions

All submissions will be acknowledged by the ABSA National Office. Applied Biosafety: Journal of the American Biological Safety Association uses a blind peer review procedure for articles, brief reports, and viewpoints. Final decisions regarding publication are made by the reviewers, Editor, and Associate Editor. The following are the guidelines for submissions. Submissions that do not conform to these guidelines will be returned to the author without review.

Submission Categories

Articles—Full-length articles may focus on the theory, practice, and research in biological safety or related areas. Articles must include an abstract of approximately 100-150 words summarizing the major point of the article.

Brief Reports—Short articles which focus on the results of research are appropriate for this section. Brief reports should include information on the research design, methods, and results. An abstract of approximately 100-150 words must also be included.

Viewpoints—Short articles focusing on personal experiences may be submitted to this section.

Book Reviews—Reviews of books of interest to biological safety may be submitted at any time. Books which authors wish to have considered for review may be sent directly to the ABSA National Office.

Video Reviews—Reviews of media (videos) may be submitted at any time. Media which producers wish to have considered for review may be sent directly to the ABSA National Office.

Commentaries—Brief comments on submissions published in Applied Biosafety, issues critical to the profession and practice of biological safety, or letters to the Editor may be submitted to this section and should conform to the style of all other submissions.

Other Requirements

1. Send five (5) typeset copies of each submission to: Editor, Applied Biosafety: Journal of the American Biological Safety Association, c/o ABSA, 1202 Allanson Road, Mundelein, IL 60060-3808, USA. Neither ABSA nor the Editor can be responsible for submissions sent to any other address. Only original submissions that are not under consideration by another periodical or publisher are acceptable.

2. Submissions should be typeset on 8-1/2" x 11" paper using 1" margins, double-spacing, and full-justification. Indent paragraphs five (5) spaces. References, footnotes, table captions, and quotations should be single-spaced. Acceptable fonts are Times New Roman, Arial, AvantGarde, Helvetica, and Universal in 12 point. Avoid dot matrix printing. Primary headings should be flush left, bolded, and have the first letter of all main words capitalized throughout the submission. Secondary headings should be flush left, italicized, and have the first letter of all main words capitalized.

3. An abstract of 100-150 words must be included with full-length articles and brief reports.


5. A cover sheet should be prepared to include the full name(s) and degree(s) of the author(s), professional affiliations, and the return mailing address of the author to whom correspondence can be sent. Authors’ names, positions, titles, and places of employment should not appear in the body of the paper to assure anonymity and to facilitate the blind review process.

6. Use tables sparingly and typeset them on separate pages. All tables, charts, or diagrams must be computer-generated or professional, quality, original drawings which are legible, able to withstand reduction, and submitted as camera ready artwork. Typeset in a vertical (portrait) format on separate pages, including any legend, label, or number associated with them. Refer to each as Table 1, Table 2, etc., centered above the table. Captions should be single-spaced. Tables, etc., should not be included in the electronic copy on diskette; however, there should be a notation of where they are to be inserted throughout the submission. Include the originals and five (5) photocopies of each with the submission.

7. Photographs must be at least 3-1/2" x 5" and black and white prints, preferably with high contrast. Photocopies of illustrations are not acceptable for publication. Figure numbers, captions, orientation, and the author’s name should be noted on the back of each original photograph. Captions must be typed and submitted on a separate sheet of paper as well. Please refer to figures in the text as Figure 1, Figure 2, etc. There should be a notation of where the photographs are to be inserted throughout the submission. Include the original figures and five (5) photocopies of each with the submission.

8. Lengthy quotations (300 words or more from one source) require written permission from the original copyright holder for reproduction. Adaptation of tables or figures from copyrighted sources also requires approval. It is the author’s responsibility to secure such permissions. A copy of the copyright holder’s written permission must be provided to the Editor immediately upon acceptance of the submission for publication. The author(s) bear full responsibility for the accuracy of all references, quotations, and materials accompanying their submissions.

9. It is expected that any submission accepted for publication in Applied Biosafety will go through at least one (1) revision before publication. Authors must include their submission on diskette (electronic copy) along with their five (5) typeset copies. The diskette should be prepared on either an IBM or IBM-compatible computer. The submission should be formatted using one of the following programs: Microsoft Word, Microsoft Publisher, or WordPerfect. ASCII II files are also acceptable.

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☐ Original tables, figures, and/or illustrations and five (5) photocopies of each.

☐ Paper and references adhere to Publication Manual of the American Psychological Association (4th ed.).

☐ Abstract of 100-150 words (for articles and brief reports only).

☐ Detachable cover sheet with author's full name(s), degree(s), professional affiliations, and credentials.

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